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A LONG-TERM STUDY ON THE USE OF APPETITE SUPPRESSANTS

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IN A PREVIOUS paper[1] a report was given on appetite suppressants in a general practice, and the conclusion was reached that appetite suppressants become ineffective after patients have been on them for some time. This return to overeating may be forestalled by shifting medication and placing the patients on a low-calorie diet. It is generally agreed that appetite suppressants are not effective in keeping weight down when used alone.[2]

The time span of an appetite-suppressant study considerably influences the results obtained. The longer the study the less effective the appetite suppressant appears to be, if the criterion of average daily weight loss is used. It was decided to investigate this effect in a long-term clinical study.

It has been observed that, of a number of people who start a clinical trial such as this one, many do not return after a few weeks. The reasons given by the subjects for not returning are of some interest and a partial answer may be found in this study. Associated with this answer is the matter of the "success" of a clinical trial.[3] At what point in the program can it be said that the regimen is successful?

METHOD

The study was conducted on a "blind" basis. As patients came to the office they were assigned, in order of their arrival, to one of four groups A, B, C and D, and were given two weeks' supply of a coded medication to be taken daily one-half hour before breakfast. The patient was placed on an active drug for eight weeks, a placebo for two weeks, and an active drug for another eight weeks. The code, which was disclosed only after completing analysis of the results, showed that two active drugs were used in various combinations. The drugs were amphetamine as cation exchange complex of sulfonated polystyrene (Am) and 2-phenyltertiarybutylamine as cation exchange (Bu). Table I lists the arrangements. Group D differed from the other groups in one respect: all the patients in this group were placed on a 1000-calorie diet in addition to receiving the medication. The diet was high in protein.

TABLE I.—DESIGN OF EXPERIMENT AND DRUG COMPOSITION

Group	*Period I*	*II*	*III*
A	Am.*	P.**	Am.
B	Am.	P.	Bu.***
C	Bu.	P.	Bu.
D	Bu. + Diet	P. + Diet	Bu. + Diet

*Am.—D- and DL- amphetamine as cation exchange resin complex of sulfonated polystyrene (Biphetamine 12.5).
**P. —Placebo.
***Bu. —2 phenyltertiarybutylamine as cation exchange resin complex of sulfonated polystyrene (Ionamin 30).

Each time the patient returned for an additional supply of medication, data were collected on weight, blood pressure, possible side effects associated with the medication, and mood. Any remarks pertinent to the study which were volunteered by the patient were also noted.

In the analysis of weight losses within each group a "sign test" was used. The sign test is a simple distribution-free test. The only assumption is the null hypothesis and the requirement that the effects to be tested are randomly distributed. The sign test is not as efficient as some statistical tests, but for large groups the loss is not important. Statistical significance by the sign test implies that more efficient tests will also indicate significance.

For example, in determining whether the weight losses of the first period of any group (see Table III) differed from those of the third period, the assumption is made that the weight losses were equal in the two periods. If a patient's weight loss in the first period exceeds his loss in the third period, a "+" is recorded; if less, a "−" is recorded; and if the same, a "O" is recorded. On the assumption of no difference, the number of "+" should be approximately equal to the number of "−" within a group. That is, the "+" and "−" are binomially distributed with probability ½ (from the null hypothesis).

The weight losses between groups were tested by the usual analysis of variance. The changes in blood pressure were also tested by the sign test.

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After completing the study certain patients wished to continue into a second round. They were reassigned in the schedule, but their results have not been included in this paper.

TABLE II.—DIVISION OF TOTAL NUMBER OF PATIENTS

Group	Total No. of patients	No. that completed the study	No. that dropped out		No. that began a 2nd round
			Did not return at all	Returned at least once	
A	60	19	13	27	1
B	59	10	21	22	6
C	59	14	16	26	3
D	59	21	16	21	1
Total	237	64	66	96	11

Results

Table II shows the division of the patients included in the study. Of 237 patients who started the study 64 completed it, while 66 did not return at all and 96 returned at least once. The patients who dropped out will be discussed in a separate section. The results, presented below, are those of the 64 patients who completed the study.

Weight Losses

The weight losses of the patients who completed the study are shown in Table III. As expected, the change in weight of the patients while on the placebo therapy was negligible. In groups A and C there was a small increase in weight of 0.4 lb. and 1.9 lb. respectively. The weight lost during the first period was significantly greater than that of the third period in all four groups, as tested by the sign test ($P<.01$).

The weight losses associated with the active drugs varied from 16.2 lb. for the first eight-week period of group D to 4.9 lb. for the second eight-week period of group D. The total weight lost in group D was 20.9 lb. as compared to approximately 16 lb. for the other three groups.

An analysis of variance of weight losses among the four groups A, B, C and D showed that the first-period weight losses of groups A, B and C were not significantly different but all were significantly less than the weight losses in group D. There were no significant differences among the third-period weight losses of all four groups.

In all cases the weight losses associated with the active drugs were significantly higher than those associated with the placebo.

Side Effects

During the 7734 patient-days of the study, 169 side effects were reported (Table IV). Of these, six side effects occurred in 928 placebo days. The most frequent side effect was dryness of the mouth which seems to be characteristic of the amphetamine-type drugs. Dry mouth accounted for 99 of the side effects, or 59%. Depression, irritability and sleeplessness constituted another 37%. The proportion of side effects does not vary from group to group, but the number of side effects in the third period is significantly less than that in the first periods. Some patients reported side effects more than once.

Alteration in Mood and Activity

For determining changes in mood an arbitrary scale was set up and used as an activity index (Table V). The scale varied from 0 to 4 for moods from depression (0) to normal (2) to definitely overstimulated (4). Very few extremes were recorded. A total of 16 marked changes were observed if 0 and 4 represent these extremes. Since the instances when the patient felt normal were obviously not always reported, the totals at the bottom of the columns and the averages give only a relative indication of the mood changes. This makes any statistical tests meaningless. In general it can be said that the patients in group D tended toward hyperactivity and that none of the drugs appears to cause depression.

TABLE III.—WEIGHT LOSS OF PATIENTS WHO COMPLETED THE STUDY

Group	No. of patients	Period	Drug*	Length of period	Average weight at: Start of period in lb.	Average weight at: End of period in lb.	Average weight loss in lb.	Weight loss per day (lb./day)
A	19	I	Am.	8 weeks	176.9	168.6	8.3	.148
		II	P.	2 weeks	168.6	169.0	− .4**	−.028
		III	Bu.	8 weeks	169.0	164.7	4.3	.080
B	10	I	Am.	8 weeks	180.2	169.0	11.2	.172
		II	P.	2 weeks	169.0	168.5	.5	.032
		III	Bu.	8 weeks	168.5	164.4	4.1	.090
C	14	I	Bu.	8 weeks	172.7	162.1	10.6	.197
		II	P.	2 weeks	162.1	164.0	− 1.9	−.126
		III	Bu.	8 weeks	164.0	158.7	5.3	.100
D	21	I	Bu. + Diet	8 weeks	187.4	171.3	16.1	.296
		II	P. + Diet	2 weeks	171.3	170.5	.8	.061
		III	Bu. + Diet	8 weeks	170.5	165.7	4.8	.103

*See Table I for the description of the drugs.
**A negative weight loss indicates a gain in weight.

TABLE IV.—SIDE EFFECTS REPORTED BY PATIENTS WHO COMPLETED THE STUDY

Group	No. of patients	Period	Drug*	Length of period	Number of times the side effect was reported: De-pressed	Irrit-able	Hyper-active	Sleep-less	Dry mouth	Edginess of teeth	Total
A	19	I	Am.	8 weeks	1 (1)†	4 (2)	2 (2)	3 (2)	19 (11)	—	29
		II	P.	2 weeks	1 (1)	—	—	—	1 (1)	—	2
		III	Bu.	8 weeks	2 (2)	4 (4)	2 (1)	5 (3)	13 (9)	—	26
B	10	I	Am.	8 weeks	2 (1)	1 (1)	1 (1)	1 (1)	13 (7)	—	18
		II	P.	2 weeks	—	1 (1)	—	—	1 (1)	—	2
		III	Bu.	8 weeks	1 (1)	1 (1)	—	3 (2)	6 (3)	1 (1)	12
C	14	I	Bu.	8 weeks	3 (3)	4 (3)	1 (1)	3 (3)	9 (6)	—	20
		II	P.	2 weeks	—	—	—	—	1 (1)	—	1
		III	Bu.	8 weeks	1 (1)	1 (1)	—	3 (2)	5 (2)	1 (1)	11
D	21	I	Bu. + Diet	8 weeks	1 (1)	2 (2)	—	6 (5)	22 (16)	—	31
		II	P. + Diet	2 weeks	—	1 (1)	—	—	—	—	1
		III	Bu. + Diet	8 weeks	2 (2)	3 (3)	—	2 (1)	9 (6)	—	16
				Total	14	22	6	26	99	2	169

*See Table I for the description of the drugs.
†Number in parenthesis is the number of patients who reported the side effect.

TABLE V.—EFFECT ON MOOD AND ACTIVITY REPORTED BY REGIMEN AND PERIOD

Group	No. of patients	Period	Drug*	Length of period	Degree of activity**: 0	1	2	3	4	Average activity
A	19	I	Am.	8 weeks	3	3	49	12	4	2.15
		II	P.	2 weeks	—	3	37	3	—	2.00
		III	Bu.	8 weeks	—	3	50	7	—	2.07
B	10	I	Am.	8 weeks	—	2	33	7	—	2.12
		II	P.	2 weeks	1	2	9	2	—	1.86
		III	Bu.	8 weeks	1	3	24	—	—	1.82
C	14	I	Bu.	8 weeks	1	2	31	12	2	2.25
		II	P.	2 weeks	1	3	19	3	—	1.92
		III	Bu.	8 weeks	2	4	27	12	—	2.09
D	21	I	Bu. + Diet	8 weeks	—	5	37	40	1	2.45
		II	P. + Diet	2 weeks	—	—	28	7	—	2.20
		III	Bu. + Diet	8 weeks	—	4	40	15	—	2.19
				Total	9	34	384	120	7	

*See Table I for the description of the drugs.
**0—Depressed
1—Slightly depressed
2—Normal activity
3—Full of energy
4—Definitely overstimulated

Blood Pressure

The changes in blood pressure for the duration of the study are given in Table VI. As was observed in an earlier paper,[1] a reduction in blood pressure is associated with the use of appetite suppressants. This is most probably due to the weight loss rather than to a pharmacodynamic effect of the drugs used.

The mean reduction in the systolic blood pressure was 3.6 mm. of Hg. This reduction was significant at the 5% level as tested by the sign test. The reduction in the diastolic blood pressure for the whole group was not significant. The mean reduction was 2.3 mm. of Hg.

The Patients Who Dropped Out

The patients who did not complete the study form a large part of the whole group. From Table II, it can be seen that 24% of these patients never returned. Those who dropped out but returned at least once make up 40% of the total number of patients starting the study. In Table VII, the distri-

TABLE VI.—AVERAGE CHANGES IN BLOOD PRESSURE

	Group	No. of patients	Mean reduction in mm. of Hg	P*
Systolic	A	18	3.0	<.01(s)
	B	10	1.4	>.05
	C	14	7.6	<.05(s)
	D	20	2.4	>.05
	Total	62	3.6	<.05(s)
Diastolic	A	18	4.0	<.05(s)
	B	10	.12	>.05
	C	14	−.43**	>.05
	D	20	.60	>.05
	Total	62	2.3	>.05

*P—Probability that the blood pressure did not change; tested by the sign test.
**—The negative sign indicates an increase in blood pressure.
(s)— indicates a significant reduction in blood pressure.

TABLE VII.—DIVISION OF THE NUMBER OF PATIENTS WHO DROPPED OUT BUT RETURNED AT LEAST ONCE

	No. of patients who dropped out in period			
Group	*I (8 weeks)*	*II (2 weeks)*	*III (8 weeks)*	*Total*
A	15	5	7	27
B	13	5	4	22
C	15	3	8	26
D	19	1	1	21
Total	62	14	20	96

bution of this 40% is given. The majority dropped out in the first period: 62 out of 96; 14 and 20 dropped out in the second and third periods respectively.

In Table VIII, first-period weight losses are listed for patients who dropped out in this period and those who completed the first period. If the weight losses of the patients who completed the first period are compared with the results from Table III, it can be seen that they are also substantial; all exceed 10 lb.

TABLE VIII.—AVERAGE WEIGHT LOSS IN LB. OF PATIENTS WHO DROPPED OUT BUT RETURNED AT LEAST ONCE, IN THE FIRST PERIOD

	Patients who	
Group	*Completed Period I*	*Dropped out in Period I*
A	10.5 (12)*	7.8 (15)
B	11.1 (9)	4.0 (13)
C	13.5 (11)	7.0 (15)
D	13.5 (2)	10.0 (19)

*Number of patients.

The side effects in this group occurred approximately as frequently as in the group who completed the study. With the small number of side effects involved it is not possible to establish statistical significance. No unusual side effects were reported by this group of patients.

DISCUSSION

The greater weight losses in the first period of all four groups A, B, C and D are not necessarily an effect of the drug used but may have other causes. A natural decrease in weight loss with time is to be expected as enthusiasm and degree of obesity decrease.

Placing the patients on a diet improved their initial weight losses. The patients on the 1000-calorie, high-protein diet (group D) lost approximately 6 lb. more than the other three groups in the first eight-week period of the study. But it must be noted that in the second-week trial the weight loss was nearly the same as that of the other groups. These results seem to imply that the diet is not adhered to after some weeks. However, the overall performance of this group is more satisfactory than that of the other three, with a weight loss 4 lb. greater. Although the proportion of patients completing the study does not vary significantly from group to group, it may be noted that the largest proportion of persons completing this study are in the group on the diet.

Some of those who did not complete the study may have stopped because they were satisfied with their weight losses. This may be true especially for the 35 patients who completed the first period only and lost approximately 12 lb. each on the average.

The side effects and alterations in mood are relatively rare. It is not known in all cases if the side effects are caused by the drug used. Unless a side effect occurs frequently, it seems more likely that it is not due to the drug used. This is borne out by some of the changes in mood. In nine instances, marked depression was reported (Table V); two of these cases occurred with placebo therapy.

It is well established that amphetamine-type appetite suppressants do not increase the blood pressure. The evidence indicates a lowering of blood pressure if there is any effect at all.

SUMMARY

A report is given on a long-term study of appetite suppressants, using two active drugs and a placebo, in four different patterns, on 237 adult patients, mostly women. The experimental period was 18 weeks. The group in one of these patterns (D), in addition to receiving the drugs, was placed on a diet of 1000 calories per day.

Both drugs are commercially available. One is an amphetamine-type drug, the other a non-amphetamine preparation.

Average weight losses for the two eight-week periods were: (a) D- and DL-amphetamine as cation exchange resin complex of sulfonated polystyrene (Biphetamine 12.5)—first period: 9.3 lb., second period: 8.1 lb.; (b) 2 Phenyltertiarybutylamine as cation exchange resin complex of sulfonated polystyrene (Ionamin 30)—first period: 10.6 lb., second period: 4.8 lb.; (c) b + 1000-calorie per day diet—first period: 16.2 lb., second period: 4.9 lb.

Side effects were few. "Dry mouth" accounted for 62% of the reported side effects.

The average systolic blood pressure declined by 3.6 mm. of Hg and the average diastolic blood pressure by 2.3 mm. of Hg during the study.

The initial and total weight loss is significantly greater when an appetite suppressant is combined with a diet.

Of the 162 patients who did not complete the study, 69 (43%) lost at least 10 lb. in varying periods of time.

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LONG-TERM ANOREXIGENIC THERAPY IN OBESE DIABETIC PATIENTS*

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A LONG-TERM study of the anorexigenic agent phenmetrazine hydrochloride (Preludin)† was begun in 1957 in the Diabetic Clinic of the Toronto General Hospital. It was designed to allow comparison with short-term studies which had been reported from other centres[1-4] with encouraging results. As this study was being concluded there appeared another optimistic short-term trial of this agent in obese maturity-onset diabetics.[5] This was a carefully controlled experiment, abstracted in this journal,[6] and purported to establish the value of the routine utilization of a pharmacologically active anorexigenic agent in the management of obesity-diabetes. In his original paper Fineberg[5] stated that the total evaluation of any therapeutic agent or modality in the treatment of obesity in diabetics must be made over a period of years, not weeks or months, and it was to this end that our study was designed.

Phenmetrazine hydrochloride is a sympathomimetic drug and congener of amphetamine. Modell[7] has classified this group of drugs as "central-stimulating appetite distractors", as distinct from "central appetite depressants" (e.g. digitalis overdosage), "metabolic stimulants" (e.g. dinitrophenol, thyroid), "sedatives and tranquillizers," "bulk producers" (methylcellulose), "purgatives and diuretics," and "miscellaneous devices," in his list of pharmacological agents for the treatment of hyperphagia. The drug was given in most cases as a 25-mg. tablet, one-half to one hour before meals, with a glass of water. Placebo tablets, identical in appearance, were substituted for the active agent in some patients, at the discretion of the physician.

In Fineberg's study,[5] 29 patients were alternated carefully with 25 control patients who received placebo tablets. Neither patient nor doctor knew the identity of the active preparation, nor were the patients told that the tablets offered to them had any effect on appetite. The average duration of the trial in his cases was *ten weeks*. Seventy-two per cent of the patients receiving phenmetrazine lost a significant amount of weight (averaging more than ½ lb. per week), as opposed to 12% in the placebo group. Fifty per cent of those taking insulin in the phenmetrazine group had their insulin requirement reduced by 50% or more.

The Toronto General Hospital patients were a considerably more heterogenous group than Fineberg's and the study did not have as effective a control with placebos. Fifty patients expressed their willingness to take pills that would help them to lose weight, in addition to their usual 1000-1200 calorie diet. They were asked to attend the clinic at monthly, instead of the customary two-monthly intervals, and they were seen on each visit by one physician. The eventual "decay-scheme" of such a group, with the smaller number finally contributing to the long-term study, seemed worth recording. Fineberg's original number of patients was 80, of which 54 were included in his final report.

TABLE I.

	T.G.H.—Group I (chronically obese and diabetic)		*Fineberg (obese, maturity-onset diabetics)*
Duration of trial	less than 6 months	more than 6 months	1-4 months (average 10 weeks)
Number of patients	10	11	29
Age:			
Range (years)	16–75	32–71	34–72
Mean age (years)	56.2	53.9	53.0
**Excess weight:*			
Range (lb.)	30–100	30–125	
Mean (lb.)	53.9	53.2	"grossly obese"

**Excess* taken to mean weight that is more than 90% of the average for age, sex and height, as published by Nutrition Division, Department of National Health and Welfare, Canada, 1953.

The 50 patients fell into four groups, the pattern of response differing slightly in each. Group I (Table I) were 29 chronically obese, long-standing diabetics who had been unresponsive to previous attempts by physician and dietitian to help them lose weight. These patients probably resembled most closely the patients in Fineberg's study. All but three of the 29 subjects were females.

Eight patients of this group were rejected for a variety of reasons. Two did not return to clinic after accepting the tablets; one claimed to have had severe diarrhea after taking only three tablets and refused to continue; one felt that the tablets produced flatulence which she found intolerable after one day, but accepted the placebo tablets; in one patient there was an aggravation of a pre-existing depression with the institution of anorexigenic therapy, which was probably coincidental; and in three edematous patients the weight charts were rendered unreliable due to variations in fluid

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†The phenmetrazine hydrochloride (Preludin) used in this study was generously supplied by Geigy Pharmaceuticals.

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TABLE II.—T.G.H.—GROUPS I AND II

	T.G.H.—Group II (*chronic obese, new diabetic*)	*T.G.H.—Group III* (*weight excess under 20 lb.*)
Number of patients	8	10 (6 for 6 mos. and longer)
Age:		
Range (years)	46-74	20-70
Mean age (years)	54.6	35
Excess weight:		
Range (lb.)	28-85	10-20
Mean (lb.)	50	18.5
Duration of trial:		
Range (mo.)	6-14	6-30
Mean (mo.)	9.7	13.6

retention. Of the remaining 21 patients, 10 received tablets for less than six months and 11 for six months to two years.

Group II (Table II) consisted of eight female patients who were chronically obese but who had *recently* been found to be diabetic. One would have anticipated better results in this group than in the previous group because of the added motivation of the new diagnosis.

Group III (Table II) was made up of 10 patients, nine females and one male, who had *less than 20 lb. excess* weight and therefore a weight goal that should not have been difficult to attain. Six of these 10 received therapy for six months and longer. One 31-year-old patient stopped taking the tablets after one week because of frequent insulin reactions. Another stopped after four months for the same reason. Two lost interest after a few months. A fifth patient continued for six months, at which time she had lost the desired amount of weight but became increasingly irritable and nervous.

The results of the long-term study are summarized in Tables IV and V. Table IV includes patients who received phenmetrazine for periods of less than six months and shows the pattern of response early in the course of the study as opposed to the pattern after six months had elapsed. Fineberg accepted weight loss of more than ½ lb. per week as being significant. If this criterion is accepted, the results of the three groups of patients in the initial two months of therapy approximated his figure of 71.9% achieving successful weight reduction. The best results (100%) were obtained in those with the least excess weight (i.e. less than 20 lb.) and the worst (62%) in the group with a large amount of excess weight, who had been overweight and diabetic for some time. The recent development of diabetes, as was predicted, did increase the frequency of success in losing weight (75%) in the group that were chronically obese. The numbers that continued to lose weight on prolonged treatment fell off sharply.

If a smaller weight loss is accepted as indicating significant reduction, the results improve but the pattern of decreasing response with increasing duration of treatment remains virtually the same. The small numbers continuing to accept therapy after 12 months are of interest but do not merit statistical analysis.

In Table V only patients who had lost weight at some time in the trial and who had remained on therapy for six months or longer are considered. It can be readily seen in all groups that 80% or more of the weight loss occurred in the first six months on the anorexigenic agent and that the great proportion of this was accomplished in the first two months.

These results confirm the favourable reports of short-term trials of phenmetrazine and other anorexigenic drugs, but suggest that there is little value in prolonged therapy. This is not a new observation.[7]

TABLE III.—T.G.H.—GROUP IV (3 OBESE PREGNANT DIABETICS)

	Age	*Height*	*Weight (lb.)*	*Weight excess (lb.)*	*Previous weight gain*	*Total gain in 3 mo. on therapy*
J.M.	30	5 ft. 4 in.	225	100	5 lb. in 4 weeks	2 lb.
I.M.	33	5 ft. 1 in.	137	20	6 lb. in 3 weeks	5 lb.
E.S.	31	5 ft. 3 in.	164	30	5 lb. in 4 weeks	10 lb. (edematous)

Group IV (Table III) consisted of three young, maturity-onset type, pregnant diabetics who were overweight, having gained excessively before starting phenmetrazine, and who had had similar excessive weight gain in previous pregnancies.

While taking phenmetrazine, these three patients were impressed by the effective control of appetite and weight. None had any side effects attributed to the drug, and their increased insulin requirements were consistent with the period of gestation.

The possible benefit of interrupted courses of phenmetrazine therapy has not been investigated. In many patients this could achieve little more than the initial attempt had achieved because of the tendency to regain the weight that had previously been lost while not under treatment. In the few patients who would keep their weight down, the cumulative effect of repeated courses of an anorexigenic drug would be worth while.

TABLE IV.—RESULT OF PHENMETRAZINE THERAPY

		Number losing		% of group losing	Number losing	% of group losing	No. with weight unchanged	No. with weight gain	Total no. of patients
	Weight loss in	more than 1 lb./wk.	1/2 - 1 lb./wk.	more than 1/2 lb./wk.	1-2 lb./mo.	more than 1 lb./mo.			
Group I	initial 2 mo.	4	9	62	4	81	3	1	21
Chronic obese	3-5 mo.	0	2	11.8	5	41	3	7	17
chronic diabetic	6-12 mo.	0	1	8	6	58	2	3	14
	over 12 mo.	0	0	0	2	33	1	3	6
Group II:	initial 2 mo.	5	1	75	1	87	0	1	8
chronic obese	3-5 mo.	1	3	50	1	62	0	3	8
new diabetic	6-12 mo.	0	2	25	2	57	1	3	8
	over 12 mo.	0	0	0	0	0	0	1	1
Group III:	initial 2 mo.	4	5	100	0	100	0	0	9
weight excess	3-5 mo.	2	1	37.5	4	87	0	1	8
under 20 lb.	6-12 mo.	0	1	20	1	40	1	2	5
*	over 12 mo.	0	0	0	2	100	0	0	2
Fineberg group	average 10 wk. range 1-4 mo.			71.9					

*Five in Group III achieved their weight goal. Four of the five lost more than one-half of the desired weight in the first two months of treatment and had reached their weight goal in six months.

Effect on Diabetic Control

There were 33 patients who lost weight at some time during the study, in whom the effect on control of their diabetes, as judged by fasting blood sugar values, tests for glycosuria between clinic visits and the occurrence of insulin reactions, could be assessed. Twelve had evidence of improved control on their previous regimen of diet, insulin, etc., coincident with weight loss. In 13 it was possible to reduce their insulin dose. Insulin was discontinued in three of these patients, but had to be resumed in two as weight was regained. The dose was significantly reduced (by 50%) in only one other patient. These results are in contrast to Fineberg's finding of 50 to 100% reduction in insulin requirement in one-half of his patients.

More striking in this study were five patients who had repeated hypoglycemic episodes when they commenced phenmetrazine therapy, despite warnings to be prepared to lower their insulin dose. The insulin reactions were sufficiently disturbing in two patients to influence them to refuse further therapy. Four of these five were growth-onset type diabetics, who were in general much more sensitive to phenmetrazine than the older, obese patients. In several instances, such patients were initially well controlled on one-half tablet (12.5 mg.) before meals and later maintained their weight loss by taking one 25-mg. tablet daily. In the maturity-onset group, on the other hand, three patients doubled the prescribed dose of phenmetrazine on their own initiative and reported failure to regain the initial anorectic effect.

Disappointing, too, was the failure of a weight loss of 10-15 lb., representing about 20% of the weight excess, to favourably effect control by diet alone in three patients. It was necessary to start these patients on insulin or on a sulfonylurea compound before the end of the study. The failure to avoid insulin injections probably contributed in some measure to the eventual decline in effectiveness of the anorexigenic drug.

TABLE V.—PATIENTS RECEIVING EFFECTIVE THERAPY FOR SIX MONTHS AND LONGER

	Average weight loss in first 2 months (lb.)		Average weight loss in 3rd-6th months (lb.)		Average duration therapy in months	Average final weight loss (lb.)	
	Total	Per month	Total	Per month		Total	Per month
Group I (11 patients)	5.5	2.7	3.1	1.03	15	12.6	.84
Group II (7 patients)	8.4	4.2	6.0	2.0	10.3	18.4	1.8
Group III (6 patients)	8.1	4.05	6.8	2.3	14.5	16.3	1.12

Side Effects

Side effects (Table VI) attributable to the central-stimulating or sympathomimetic action of phenmetrazine in this study were encountered in 12 of 48 patients or 25% (Fineberg's incidence was 14.7%). In one patient only did habituation to the stimulating effects of the drug seem to be a possibility.

One patient stopped therapy because of the appearance of a pruritic, erythematous, macular eruption on her limbs and trunk six months after beginning phenmetrazine. The rash recurred one week after it was resumed after a brief lapse.

Two patients, in whom the drug was discontinued shortly after its administration, reported

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TABLE VI.—INCIDENCE OF SIDE EFFECTS OF PHENMETRAZINE

	On active agent	*Continued on placebo*	*Severity warranted discont. Rx.*
Headache	1	0	1 (late)
Dizziness	1	0	(reduced dose)
+ Nervousness and irritability	1	0	1 (late)
+ Insomnia	3	1	0
+ Palpitations	1	0	1 (late)
Dryness of mouth	2	1	0
Diarrhea	2	0	1 (immediate)
Flatulence	1	0	1 (immediate)
Constipation	3	3	0
Skin rash (?)	1	0	1 (late—6 months)
	19 in 17 patients	5	6

gastrointestinal dysfunction which may or may not have been due to the drug. Other side effects (e.g. nervousness, irritability, headache and palpitations), sufficiently unpleasant to cause the patient to stop taking the drug, were not mentioned until several months after beginning therapy.

Effects of Placebo

This study was not conducted on a double or triple blind basis. Placebo tablets were substituted for the active preparation when side effects appeared or when weight loss on the active agent had ceased and the weight chart had a plateau-like appearance. When a placebo was given in place of the active drug, seven of eight patients in Group I and two of three in Group II gained weight. The placebo tablets were used as *initial* therapy in only two patients, both of whom lost a satisfactory amount of weight. Once again these numbers have no statistical validity but they imply an advantage for the first agent used, whether it be the active or the inactive preparation.

Other Observations

Somewhat to our surprise there were five patients in this group of 50 who deviated sufficiently from the pattern of the majority to warrant special mention.

After four months of therapy, one patient (in Group I), as previously mentioned, frankly admitted that her interest in continuing the tablets was derived from the extra "lift" and energy she attributed to them. At a later date she was given diethylpropion hydrochloride* and was disappointed because it did not give her the desired "lift".

Two patients, one in Group I and one in Group III, with marked weight excess (100 lb. and 60 lb.) and younger than the average age for their groups (31 and 47 years), started the new tablets with great enthusiasm and were most-co-operative about keeping monthly appointments. In the first two months one lost 11 lb. and the other gained 1 lb. In the next three months both gained steadily. Although they had been in regular attendance at various outpatient clinics, neither could be persuaded by any means to cross the threshold of the hospital again. The extra attention to weight loss had apparently struck a much more vulnerable spot than had the impersonal approach of previous years.

Another 47-year-old, 5′ 2″ woman who weighed 176 lb. at the beginning of the study lost 20 lb. in the first four months and was gratified to be able to discontinue her insulin injections (6 units P.Z.I.). In the succeeding 12-month period she neither gained nor lost significant weight; then while still on phenmetrazine, she began to gain rapidly and had to resume insulin at twice her previous dose. She was observed for a further 18 months, in which time her weight increased to 183 lb. and her diabetic control deteriorated. She was given diethylpropion and the long-acting phenmetrazine preparation which became available, without benefit. This patient apparently used weight gain, rather than loss, to centre attention upon herself and her domestic problems, because she hoped to barter community financial assistance, which she was not eligible to receive, for her continued co-operation in the project of weight control.

The fifth patient of particular interest was a 20-year-old, 5′ 6″ tall, 137-lb. girl who had gained 20 lb. in the previous year with detrimental effect on her diabetic control. She began to take phenmetrazine in a casual manner, needing only one tablet daily to curtail her between-meal eating habits, and lost 17 lb. over a nine-month period. In retrospect her weight loss increased in tempo, unlike the usual pattern in which the maximum loss occurred in the early months of therapy. Although she had more than achieved her goal, she continued to lose weight without medication and was subsequently admitted to hospital weighing 89 lb. with a diagnosis of anorexia nervosa.

SUMMARY

A long-term study of the anorexigenic amphetamine congener, phenmetrazine hydrochloride, was designed to allow comparison with short-term trials, which have been favourably reported previously.

The subjects were diabetic outpatients who could be classified into three groups according to weight excess and duration of diabetes.

Patients with less than 20 lb. excess weight and patients recently found to be diabetic had a more satisfactory weight reduction than those who had been both diabetic and obese for some time. However, almost all of those who lost weight did so most effectively during the first two months on the drug and had almost achieved their maximum loss in six months. Prolongation of therapy beyond this time had little to offer. Weight control, i.e. reduction in rate of gain in weight, was satisfactory in three diabetics in the final trimester of pregnancy, who formed a fourth group.

*Diethylpropion (Tenuate), kindly supplied by William S. Merrell Co.

Diabetic control generally, but not invariably, improved with weight reduction. This was most apparent among the younger insulin-sensitive patients in whom insulin reactions at the beginning of therapy were often a problem.

Side effects were encountered in 25% of patients, and were responsible for discontinuance of the drug (although often after several months) in 12.5%. Weight loss was effected with a placebo in the two cases in which it was the initial therapy.

Unusual modes of responses to anorexigenic therapy in five patients in this study are noted.

The author is indebted to Dr. R. F. Farquharson for his interest and advice.

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PREDIABETES AND PREGNANCY*

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IT IS ACCEPTED that when diabetes and pregnancy coexist, such complications as toxemia, late intrauterine death of the fetus, premature labour, and fetal gigantism may occur. In the babies which survive the delivery, difficulties in the nursery are encountered.[3, 11] Sucking and respiratory problems are similar to those seen in undersized premature babies. Some observers report an increased number of congenital abnormalities, although this feature has not been noted by others. In the babies who do not survive, definite pathological findings have been well documented. These include cardiomegaly, hepatomegaly, enlargement of the islets of Langerhans, and extramedullary hematopoiesis.[18-21] A similarity to the pathological findings in erythroblastosis has been noted.[11]

These findings do not seem to be strictly related to the severity of the diabetes or the level of the blood sugar. They have been reported in association with the prediabetic state. Jackson[8] has reported a 14% incidence of stillbirths in prediabetic mothers compared with a 5% incidence in control mothers. Others have noted similar fetal and neonatal losses in some series exceeding 30%. In spite of improvement in care of the mother and early delivery by the method of choice in indicated cases, the overall perinatal death rate has remained from 5 to 7% and the morbidity has remained high.

Considerable experimental and clinical work has been done which indicates that the prediabetic state is a definite clinical entity and that it exists for many years prior to the time when a clinical diagnosis can be made by present methods of testing. Some believe that this state may exist from the moment of conception. Pregnancy, infection, puberty, obesity and steroid therapy are all examples of stressful situations associated with decreased carbohydrate tolerance. Pregnancy is one of the periods during which the first manifestations of a prediabetic state may be brought to light. Therefore the prediabetic state is not only of great academic interest, but every obstetrician should be aware of its clinical features and implications.

This concept of a prediabetic state has either been not completely accepted or is poorly understood in some areas. The fault may be due partially to the indifference of many internists to the obstetrical aspect of the syndrome, since these mothers do not need insulin to "balance" their diabetes *per se*. Additional confusion results from the lack of detailed knowledge of the normal values for the oral glucose tolerance curve during pregnancy, and by the differences in opinion regarding the significance of minor variations in curves which are only "slightly beyond the range of normal". Some very practical applications of information, which have accumulated since Allen's publication[21] in 1939, have been lost in the argument over semantics, such as whether a given curve is diabetic or prediabetic.

In the eight-year period from 1951 to 1958 there were 70 "frank" diabetics documented in 33,259 deliveries at the Women's Pavilion of the Winnipeg General Hospital. During this same period only one prediabetic (or acceptable equivalent synonym) was recorded, and on the basis of the information provided in the record even this one case was not soundly documented. One can only infer that the low recorded incidence of prediabetes in this institution is due to poor documentation or may reflect a general opinion that the unfavourable obstetrical features associated with this syndrome have been overemphasized. Because of this observation, a project was designed for the purpose of documenting the local experience in a group of pregnant patients under close scrutiny. The group under study consists of all patients who attended the prenatal clinic or were confined on the public (staff) service from July 1, 1958, to June 30, 1959. This group consisted of 642 women who had 670 pregnancies. The studies are being continued to enlarge on the initial experiences obtained in this preliminary report.

METHOD

A glucose tolerance curve was requested if glycosuria was noted at any time during pregnancy or if the history suggested prediabetes. Features such as family history of diabetes, oversized infants,

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previous unexplained perinatal losses, repeated miscarriages and hydramnios were considered suggestive. All patients received an initial complete urinalysis with a subsequent urinalysis for albumin at each visit. Prior to January 1, 1959, the urine was checked subsequently for sugar only in each trimester unless specifically requested. After the latter date the urine was checked for sugar on each visit. The standard 50-g. oral glucose tolerance test was used and the values for "true" glucose were measured. Where possible the patient was placed on a preparation diet consisting of at least 3000 calories including 300 g. of carbohydrate for three days prior to the test.

In some cases where the patient did not report for prenatal care until shortly before the onset of labour, an attempt was made to obtain a curve within the first 48 hours following confinement. When an "abnormal" curve was obtained at any time in the prenatal period, a repeat curve was requested on the sixth postpartum day.

Normal Carbohydrate Tolerance and Renal Thresholds in Pregnant and Non-pregnant Women

Normal values for the oral glucose tolerance curve in the non-pregnant individual are up to 100 mg., 160 mg. and 100 mg. % for the fasting, peak and two-hour levels respectively, by methods estimating "true" glucose values. The generally accepted renal threshold is 150 ± 5 mg. %.

The "normal" curve for pregnancy has until recent years not been fully appreciated. The values for the oral glucose tolerance curve remain within normal limits, based on non-pregnant levels, throughout the entire pregnancy except for a slight increase in the mean levels at the two-hour and three-hour readings. Lund and Weese[16] state that in some cases, the fasting, one-half hour and one hour levels may be slightly lower. In association with the test, there may be glycosuria, as lowering of the renal threshold is not uncommon. When this phenomenon does occur, it may be progressive during the pregnancy and may become more marked in each trimester. Therefore glycosuria is most common in the second and third trimesters. This renal glycosuria may complicate the management of the pregnant diabetic with resulting imbalance, ketosis, acidosis and hypoglycemic reactions. The incidence of renal glycosuria in pregnant diabetics is unknown.[24] There has been some suggestion that, in the normal patient, renal glycosuria may be the forerunner of diabetes,[25] but this has not been generally accepted. At the present time, the significance of this finding in the pregnant patient is unknown. The mechanism of renal glycosuria in pregnancy is discussed by Smith.[25] The renal threshold may be increased in some patients during pregnancy, and glucose may be absent from the urine despite an abnormal tolerance curve.

Disturbances of carbohydrate metabolism may become worse in each trimester, and when there is any disorder in carbohydrate tolerance before pregnancy the difficulty is accentuated during pregnancy. In most cases the loss of carbohydrate tolerance improves or ceases shortly after confinement, in many cases within 24 hours. Carrington, Shuman and Reardon[2, 3] believe that glucose tolerance curves, obtained more than 24 hours after confinement, become increasingly less informative with passage of time. Where decreased carbohydrate tolerance does occur, it tends to repeat itself in successive pregnancies. Hoet[7] believes that pregnancy imposes a functional burden on the islets of Langerhans and on the production of insulin. He states that the precise cause of the alteration is not known, but it is postulated that placental production of corticotrophin and increased maternal blood levels of corticosteroids found in pregnancy may be factors.

In non-pregnant individuals Conn[5] considers any person to be a diabetic whose glucose tolerance curve shows a blood sugar level (Sömögyi) greater than 160 mg. % in the first hour, 140 mg. % at one and one-half hours and 120 mg. % at two hours. A curve below 160 mg. % in the first hour and 110 mg. % in two hours is considered normal. When the two-hour blood sugar reading lies between 110 and 120 mg. %, he classifies the curve as "probably diabetes". He states that these findings are in close agreement with those of Mosenthal and Barry[22] and Moyer and Womack,[23] and that in his studies over a 25-year period this "160, 140, 120" criterion has never failed.

Jackson[8-11] feels that any lowering of the carbohydrate tolerance during pregnancy is probably abnormal, and has established what he considers the normal glucose tolerance curve for the 36th week and the sixth postpartum day. Using the Hagedorn-Jensen method, values less than 120 mg. % fasting, below 200 mg. % at the peak, below 140 mg. % at two hours, and below 130 mg. % at two and one-half hours were considered within normal limits. In terms of "true" glucose values these can be seen to approximate very closely those in the non-pregnant individual, defined by Conn.[5]

Carrington, Shuman and Reardon[2, 3] also consider any elevation of the blood glucose values above those for the non-pregnant glucose tolerance curve as significant. They divide their abnormal curves into three groups based on the value for the two-hour blood sugar (Folin-Wu) as follows:

Group I.... 120 to 140 mg.%: "suggestive of diabetes".
Group II.... 140 to 170 mg.%: "prediabetes".
Group III.... over 170 mg.%: "frank (gestational) diabetes".

Definition of Normal Curve

As various authors do not agree on the exact upper limit of normal for the blood glucose values, the following arbitrary subdivisions have been made strictly for the purpose of correlating the findings in this series with a mild, moderate or severe abnormality of the glucose tolerance curve. The upper limits of normal for the fasting and peak levels were

TABLE I.—DISTRIBUTION OF PATIENTS

Group	*Criteria*	*No. of patients*	*%*
Control	No glycosuria No curve or normal curve	476*	74.1
Renal glycosuria	Glycosuria Normal curve	47	7.3
Glycosuria undiagnosed	Glycosuria No curve obtained	43†	6.7
Abnormal	As defined in Table II§ excluding previously known diabetics	41‡	6.4
Previously known diabetics		3	0.5
Excluded	No curve, confined elsewhere	32	5.0
		642	100.0

*500 pregnancies
† 45 pregnancies
‡ 43 pregnancies
§ 1 did not return—lost to follow-up.

taken at 100 mg. % and 160 mg. % respectively. Subdivision into four groups has been based mainly on the figures for the two-hour blood sugar determinations even though the degree of abnormality of a curve is not related to this determination alone. Curves showing two-hour values of 140 mg. % or greater were considered frankly diabetic. Values between 120 and 139 mg. % were considered prediabetic. Values between 110 and 119 mg. % were considered "probably" prediabetic and those between 100 and 109 mg. % as "questionable" prediabetes.

RESULTS

The individual curves and the distribution into groups, on this basis, are shown in Tables I, II and III. In eight cases where the fasting and two-hour blood sugar values were normal but the upper limit for the peak was exceeded, this was considered a mild abnormality and was included in Group I. It is quite likely that future work based on the values obtained by an intravenous glucose tolerance method may alter some of the findings of this and similar studies based on oral glucose tolerance testing.

Forty-seven subjects showed sugar loss in the urine during pregnancy with a normal glucose tolerance curve. Forty-three cases in which a glucose tolerance curve was not obtained for various reasons have been listed as "undiagnosed" glycosuria. No glycosuria was noted in 476 cases. In this group either no curve was done or, if a curve was done for reasons other than the presence of glycosuria, it was found to be within normal limits. This group was used as the control group. As the significance of renal glycosuria in the pregnant and nonpregnant individual is still disputed, none of these cases was included in the control group. Advantage has been taken of the opportunity to compare the 47 cases in this group with the other three groups. Thirty-three patients failed to return for confinement after a variable number of prenatal visits and were lost to follow-up. Of these, one (Case 6) had an abnormal curve and was included in the abnormal group. The other 32 patients could not be included in any group and have been excluded.

TABLE II.—DISTRIBUTION OF ABNORMAL CURVES

Group	*2-hr. blood sugar mg.% (Sömögyi)*	*No. patients*	*%*
I. Questionable prediabetes	100-109	18	43.9
II. Probably prediabetes	110-119	14	34.1
III. Prediabetes	120-139	9	22.0
IV. Diabetes	140 and over	0*	

*One patient in group I and one patient in group III showed frankly diabetic curves before the end of the pregnancy.

Excluding three previously known diabetics, only one patient (Case 40) received insulin therapy when the curve at 35 weeks of gestation became frankly diabetic (F.B.S. 148 mg. %). Otherwise no treatment was directed at the prediabetes *per se*. The treatment given was the standard prenatal care in this institution, and any complications of the pregnancy were treated for the obstetrical indication and not on the basis of an abnormality of the glucose tolerance curve.

Age Distribution

The age distribution of the patients in each group is shown in Table IV. The modal class in the control group is age 20 to 24. The modal class in the abnormal group is age 25 to 34. The probability is 0.1 when examined by the chi square test. This is not significant but is suggestive that there is a difference in the age distribution of the two groups. There is no significant difference between the age distributions of the renal glycosuria and the "undiagnosed" glycosuria groups when compared with the control group. This is in accordance with what would be expected from the increasing incidence of diabetes known to occur with age. Thorn and Forsham[26] report the peak incidence of diabetes in the 50 to 59 year age group. The peak in the other three groups is more closely related to the peak incidence of pregnancy which has been reported by Logan[15] as 25 years of age.

Gravidity

The distribution of each group of patients according to the number of previous pregnancies is shown in Table V. Forty-one per cent of the patients in the abnormal group were pregnant for at least the sixth time compared with 24% in the control group. The difference is significant ($P = 0.05$). In the other two groups the number of women pregnant for at least the sixth time is more closely related to the control group. In statistics from England and Wales reported by Logan[15] only 4.5% of normal women were pregnant for at least the sixth time. The difference in the control group in this series and that of Logan may be related to differences in age distribution, and racial or socio-economic

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TABLE III.—INDIVIDUAL CURVES

No.	Age	Parity P	Parity G	Time of curve (weeks)	Antepartum curve—hours 0	1/2	1	2	3	Group	Time (days)	Postpartum curve—hours 0	1/2	1	2	3
1	28	4	5	39	76	121	172	96	56	I	—	—	—	—	—	—
2	25	2	4	40	77	125	133	102	79	I	6	72	114	101	75	64
3	30	2	3	37	74	135	143	128	75	III	5	69	146	171	78	55
4	34	7	11	20	75	109	129	136	71	III	—	—	—	—	—	—
5	39	11	12	—	—	—	—	—	—	II	6	84	169	177	112	—
6	18	0	1	36	81	129	120	134	79	III	—	—	—	—	—	—
7	33	3	4	37	85	160	200	117	80	II	6	82	148	213	103	60
8	25	2	3	11	83	127	137	117	98	II	6	78	159	176	110	55
9	23	2	3	33	93	—	—	134	—	III	3	82	118	133	75	60
10	30	1	2	38	86	168	137	67	67	I	—	—	—	—	—	—
11	31	6	7	37	84	144	156	120	69	II	42	80	105	115	111	67
12	32	4	5	30	91	168	125	72	72	I	6	79	112	112	54	56
13	18	0	1	39	86	96	120	115	62	II	—	—	—	—	—	—
14	37	4	4	—	—	—	—	—	—	I	3	78	127	142	100	65
15	35	5	7	37	77	163	220	110	62	I	1	67	160	163	134	77
16	32	8	9	37	80	178	215	103	63	I	—	—	—	—	—	—
17	40	12	13	29	101	168	211	91	62	I	—	—	—	—	—	—
18	17	0	1	26	91	127	160	106	102	I	6	91	153	172	144	125
19	26	3	5	37	80	138	159	114	78	II	—	—	—	—	—	—
20	22	0	1	34	77	104	146	115	64	II	—	—	—	—	—	—
21	27	6	7	39	72	114	124	123	72	III	6	79	102	93	89	84
22	23	4	5	26	85	152	188	118	104	II	6	92	148	120	66	65
23	19	0	2	34	87	102	136	124	86	III	2	68	96	120	88	60
24	29	6	8	33	80	132	174	86	56	I	6	71	111	170	58	55
25	28	6	7	—	—	—	—	—	—	I	2	74	138	194	90	51
26	26	3	4	—	—	—	—	—	—	III	2	69	112	113	130	60
27	30	5	6	38	73	125	150	120	60	II	5	68	113	103	50	60
28	16	0	1	29	64	89	105	102	96	I	4	68	142	138	70	58
29	27	8	9	37	77	108	145	140	78	III	6	76	127	195	116	60
30	28	4	12	38	70	91	107	116	88	II	—	—	—	—	—	—
31	25	9	12	35	73	123	135	113	73	II	6	80	113	155	93	67
32	22	1	2	—	—	—	—	—	—	II	4	80	144	118	118	50
33	22	2	3	39	66	78	70	106	54	I	—	—	—	—	—	—
34	17	0	1	32	83	132	128	102	72	I	2	79	137	132	90	68
35	18	1	2	40	81	132	120	115	72	II	—	—	—	—	—	—
36	19	1	2	11	79	164	184	118	102	II	—	—	—	—	—	—
37	37	5	7	41	80	164	168	98	68	I	—	—	—	—	—	—
38	36	8	10	—	—	—	—	—	—	I	5	69	125	192	86	57
39	24	0	1	36.5	89	142	136	100	81	I	—	—	—	—	—	—
40	30	7	8	25	96	163	211	134	81	III	2	103	—	—	—	—
											5	76				
41	37	3	4	—	—	—	—	—	—	I	4	75	183	183	85	58

TABLE IV.—AGE DISTRIBUTION

Age	Abnormal No.	Abnormal %	Renal glycosuria No.	Renal glycosuria %	"Undiagnosed" glycosuria No.	"Undiagnosed" glycosuria %	Control No.	Control %
15-19	8	19.5	8	17.0	6	14.0	94	19.7
20-24	5	12.2	21	44.7	13	30.2	139	29.2
25-29	11	26.8	9	19.1	12	27.9	109	22.9
30-34	11	26.8	7	14.9	8	18.6	71	14.9
35 plus	6	14.6	2	4.3	4	9.3	63	13.2
	41		47		43		476	

TABLE V.—GRAVIDITY

Pregnancy	Abnormal No.	Abnormal %	Renal glycosuria No.	Renal glycosuria %	"Undiagnosed" glycosuria No.	"Undiagnosed" glycosuria %	Control No.	Control %
1st	7	17.1	12	25.5	8	18.6	102	21.4
2nd	5	12.2	4	8.5	9	20.9	80	16.8
3rd	5	12.2	14	29.8	4	9.3	72	15.1
4 - 5	7	17.1	8	17.0	11	25.6	108	22.7
6 plus	17	41.4	9	19.2	11	25.6	114	23.9
	41		47		43		476	

TABLE VI.—HISTORY OF PREVIOUS FETAL LOSSES*

Fetal losses	Abnormal No.	Abnormal %	Renal glycosuria No.	Renal glycosuria %	"Undiagnosed" glycosuria No.	"Undiagnosed" glycosuria %	Control No.	Control %
Types:								
Abortion—1	8/34	23.5	4/35	11.4	5/35	14.3	60/374	16.0
Abortion—1+	4/29	13.8	2/31	6.5	5/26	19.2	43/294	14.6
Intrauterine death—1	1/34	2.9	0	—	2/35	5.7	16/374	4.3
Intrauterine death—1+	0	—	0	—	0	—	2/294	0.7
Neonatal death—1	2/34	5.9	2/35	5.7	1/35	2.9	18/374	4.8
Neonatal deaths—1+	1/29	3.4	0	—	0	—	4/294	1.4
Total:								
Fetal loss—1	14/34	41.1	7/35	20.0	11/35	31.7	128/374	34.2
Fetal losses—3+	4/24	16.7	2/17	11.8	2/22	9.1	23/222	10.4

*This table and all the following tables where necessary have been corrected for gravidity.

factors. The marked difference between the control group and the abnormal group in this series suggests that some other factor is present in the latter group. Hoet[7] and others believe that pregnancy imposes a functional burden on the islets of Langerhans and that carbohydrate tolerance improves or reverts to normal shortly after confinement. The suggestion has been made that pregnancy leaves some residual deficit, thus hastening the onset of clinical carbohydrate intolerance at a later date and with the appearance of diabetes earlier than it would otherwise have become clinically evident. However, in this study the number of patients with abnormal curves is small, no long-term follow-up is available, and there has been no adequate control of the other previously mentioned relevant factors. Therefore at the present time no statement as to the cause of this significant difference can be made.

History of Previous Fetal Losses

The number of abortions, intra-uterine deaths and neonatal deaths previous to the present pregnancy is shown in Table VI. In the abnormal group 35.3% of the women gave a history of at least one abortion compared with 27.5% in the control group. A greater percentage of women in the control group gave a history of more than one abortion. Fewer women in the abnormal group gave a history of a previous stillbirth than in the control group, and there were no women in the abnormal group with a history of more than one stillbirth. This is not in accordance with the results reported in the literature by Jackson[8-14] and others.

In the abnormal group 8.8% of women gave a history of at least one neonatal death and 3.4% gave a history of more than one neonatal death. In the control group the respective figures were 5.8% and 1.4%.

In the abnormal group 41.1% gave a history of at least one fetal loss and 16.7% gave a history of three or more fetal losses compared with 34.2% and 10.4% respectively in the control group. In this small series there is no statistical difference in the history of fetal losses per patient in the abnormal and control groups. However, the trend is in the direction of an increased history of fetal losses per patient in the abnormal group, in accordance with the findings reported in the literature.

Family History of Diabetes

The incidence of a positive family history of diabetes is shown in Table VII. In many cases there is no definite recorded statement regarding family history of diabetes. In most cases this is the result of recording positive information only. However, as there is no way of knowing in how many cases the historian has completely neglected to obtain the information, the negative histories have been further subdivided showing the number of definite denials of a positive family history.

TABLE VII.—FAMILY HISTORY OF DIABETES

	Abnormal		*Renal glycosuria*		*"Undiagnosed" glycosuria*		*Control*	
	No.	*%*	*No.*	*%*	*No.*	*%*	*No.*	*%*
Positive	7	17.0	2	4.3	1	2.3	19	4.0
Negative	20	48.8	19	40.4	9	20.9	78	16.4
Not recorded	14	34.1	26	55.3	33	76.7	379	79.6
	41		47		43		476	

In the abnormal group a positive family history of diabetes was obtained in 17% compared with 4% in the control group and less than 5% in both other groups with glycosuria. The increased incidence of a family history of diabetes in the abnormal group is significant when compared with the control group ($P = 0.001$). The lower percentage of positive family histories in the renal glycosuria and "undiagnosed" glycosuria groups as well as in the control group suggests that the higher incidence in the abnormal group is not simply due to attraction of the historian's attention by the glycosuria. When the renal glycosuria and "undiagnosed" glycosuria groups are compared with the abnormal group, the increased incidence of a positive family history in the latter group is still significant ($P = 0.02$).

Toxemia

The incidence of a previous history of toxemia and the incidence of toxemia in the present pregnancy are shown in Table VIII. Both are higher in the abnormal group than in the control group. In the abnormal group 14.7% of the women gave a history of a previous episode of toxemia compared with 4.8% in the control group. In the present pregnancy there was evidence of pre-eclamptic toxemia in 47.5% of the abnormal group compared with 14.3% in the control group. The difference is highly significant ($P = <0.001$). There is no significant difference in the incidence of toxemia in either the renal glycosuria or the "undiagnosed" glycosuria groups when compared with the control group. All cases of pre-eclamptic toxemia in the present pregnancy are based on definite evidence of at least two of the three cardinal requisites: elevation of blood pressure, excessive weight gain or edema, and albuminuria. There was no case of eclampsia in any of the groups. The majority of the cases of pre-eclamptic toxemia were mild and were treated with rest, mild sedation, salt restriction and non-mercurial diuretics (chlorothiazide and hydrochlorothiazide).

TABLE VIII.—INCIDENCE OF TOXEMIA

	Abnormal		*Renal glycosuria*		*"Undiagnosed" glycosuria*		*Control*	
	No.	*%*	*No.*	*%*	*No.*	*%*	*No.*	*%*
History in previous pregnancy	5/34	14.7	4/35	11.4	2/35	5.7	18/374	4.8
Present pregnancy	19/40	47.5	3/47	6.2	4/43	9.3	68/476	14.3

Onset of Labour

The time and manner of onset of labour is shown in Table IX. Labour was induced in 10% of the

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TABLE IX.—TYPE AND TIME OF ONSET OF DELIVERY

Type of onset	*Abnormal* No.	%	*Renal glycosuria* No.	%	*"Undiagnosed" glycosuria* No.	%	*Control* No.	%
Spontaneous	36	90	43	93.5	43	95.6	457/487†	93.8
Induced:								
Pitocin	0	—	0	—	0	—	3/487	0.6
Artificial rupture of membranes	4	10	3	6.5	2	4.4	20/487	4.1
Time of onset								
<28 wks. (<750 g.)	0	—	0	—	1	2.2	13/500	2.6
<28 wks. (>750 g.)	0	—	0	—	0	—	7/500	1.4
28-37 wks.	0	—	7	15.2	5	11.1	55/500	11.0
38+	40	—	39	84.8	39	86.7	425/500	85.0
	40*	—	46	—	45	—	—	—

*Three confined elsewhere. †Corrected for 13 miscarriages.

group with abnormal curves and in 4.7% of the control group. The slightly higher percentage in the former group is mainly due to the greater incidence of toxemia in this group, since the majority of inductions in both groups were for pre-eclamptic toxemia. In the abnormal group three of the four inductions and in the control group 15 of the 20 inductions were for pre-eclamptic toxemia.

In the control group 85% of the pregnancies were of at least 38 weeks' duration. Eleven per cent were between 28 and 37 weeks' duration and 1.4% were of less than 28 weeks' duration, with theoretically viable infants (more than 750 g.). In the abnormal group, all of the pregnancies were at least of 38 weeks' duration. This finding is not what one would expect in this series in view of the increased incidence of toxemia and the increased incidence of induction of labour in the abnormal group. Since the three inductions for toxemia in this group were carried out at term and there were no cases of eclampsia, it seems obvious that none of the cases of toxemia in the induced or non-induced groups of the abnormal patients became a problem at a time when fetal viability was jeopardized to any great extent.

Further study in a larger series of the apparent mild nature of the toxemic process in the abnormal group is warranted with better control of age distribution and other related factors. Exaggeration of the decreased carbohydrate tolerance of normal pregnancy has been reported in association with toxemia.[1] Twenty-eight of the 41 abnormal curves in this group were obtained after the 28th week of pregnancy. The possibility that some of the milder abnormal curves are secondary to the toxemia rather than primary indicators of a true prediabetic state cannot be excluded at the present time.

Method of Delivery

The manner of delivery in each group is shown in Table X. In this series there were no Cesarean sections in the abnormal group and nine (1.8%) in the control group. The proportion of breech deliveries is almost equal in the control and abnormal groups. The number of cephalic deliveries that were assisted with forceps was less in the abnormal group than in the control group. In the latter group 22.6% of the cephalic deliveries were assisted with forceps compared with 18.4% of the cephalic deliveries in the abnormal group.

TABLE X.—METHOD OF DELIVERY

	Abnormal No.	%	*Renal glycosuria* No.	%	*"Undiagnosed" glycosuria* No.	%	*Control* No.	%
Cephalic								
spontaneous	31	77.5	32	69.6	33	73.3	352	72.3
assisted	7	17.5	12	26.1	12	26.7	103	21.1
Breech	2	5.0	1	2.2	0	—	23	4.7
Cesarean section	0	—	1	2.2	0	—	9	1.8

History of Large Babies

The incidence of large children is shown in Table XI. In the abnormal group 33 women had previously given birth to 22 babies weighing more than 9 lb. and to five babies weighing more than 10 lb. In the renal glycosuria group, 35 women had given birth to 12 babies weighing more than 9 lb., to four babies weighing more than 10 lb., and to one baby over 11 lb. In the control group 374 women had given birth to 106 babies weighing over 9 lb., to 18 babies weighing over 10 lb. and to three babies weighing over 11 lb.

TABLE XI.—HISTORY OF LARGE BABIES

	Wt. (lb.)	*Abnormal* No.*	%	*Renal glycosuria* No.	%	*"Undiagnosed" glycosuria* No.	%	*Control* No.	%
None	>8	13/34	38.2	15/35	42.9	18/37	48.6	298/374	79.7
	9+	13/34	38.2	11/35	31.4	7/37	18.9	76/374	20.3
	10+	5/34	14.7	4/35	11.4	3/37	8.1	17/374	4.5
	11+	0	—	0	—	1/37	2.7	3/374	0.8
More than one	9+	6/29	20.7	1/31	3.2	2/26	7.7	18/294	6.1

In the abnormal group 14.7% of the mothers had given birth to at least one child weighing 10 lb. or more, compared with 4.5% in the control group. In the abnormal group 38.2% of the mothers had given birth to at least one child weighing 9 lb. or more, and 20.7% had given birth to more than one. In the control group 20.3% of the mothers had given birth to at least one child weighing 9 lb. or more and 6.1% to more than one. There is a significant difference in the number of women in the abnormal group who had given birth to more than one baby weighing more than 9 lb. ($P = 0.02$).

In the abnormal group 38.2% of the mothers had not previously given birth to a child weighing more than 8 lb. compared with 79.7% of the mothers in the control group.

Birth Weights of Babies in Present Pregnancy

The birth weights of the babies born in the present pregnancy are shown in Table XII. In the abnormal group 26.8% of the viable babies born weighed 9 lb. or more and 7.3% weighed 10 lb. or more, compared with 8.3% and 2.0% respectively in the control group. There were no babies weighing 12 lb. or more in the control group and 0.2% of the babies weighed 11 lb. or more compared with 2.4% and 4.9% respectively in the abnormal group. When the number of babies weighing over 9 lb. in the abnormal group is compared with the control group the difference is significant ($P = <0.001$).

TABLE XII.—BIRTH WEIGHTS IN PRESENT PREGNANCY

Weight (lb.)	*Abnormal*		*Renal glycosuria*		*"Undiagnosed" glycosuria*		*Control*	
	No.	*%*	*No.*	*%*	*No.*	*%*	*No.*	*%*
< 5.5	1	2.4	1	2.2	1	2.3	55	11.1
5.5 - 8.9	29	70.7	37	80.4	39	90.7	400	80.6
9 - 9.9	8	19.5	5	10.9	2	4.7	31	6.3
10 - 10.9	1	2.4	3	6.5	1	2.3	9	1.8
11 - 11.9	1	2.4	0	—	0	—	1	0.2
12+	1	2.4	0	—	0	—	0	—
9+	11	26.8	8	17.4	3	7.0	41	8.3
	41		46		43		496	

One of the women in the control group who gave birth to a baby weighing more than 10 lb. had previously given birth to two children weighing more than 9 lb. (one more than 10 lb.) and had a previous fetal loss. In her next pregnancy she was toxemic and delivered twins spontaneously, both of which died in the neonatal period. However, she did not show glycosuria during the pregnancy in this study and there was no record of a glucose tolerance curve. Two other women in the control group who gave birth to babies weighing over 9 lb. developed glycosuria in the following pregnancy. There is no significant difference in the number of babies weighing over 9 lb. born to the mothers in the renal glycosuria and the "undiagnosed" glycosuria groups when compared with the control group.

Multiple Pregnancy and Congenital Abnormalities

The frequency of multiple pregnancy and congenital abnormalities in the present and previous pregnancies is shown in Table XIII. In the present pregnancy the frequency of multiple pregnancy was 2.6% for the abnormal group and 1% for the control group. A higher percentage of women in the abnormal group gave a history of previous multiple pregnancy. No women in the abnormal group gave a history of a previous congenital abnormality. In the present pregnancy, one woman in the latter group gave birth to a microcephalic child (2.6%), equalling the percentage in the control group. However, the series is too small to draw any conclusions regarding these two features.

TABLE XIII.—MULTIPLE PREGNANCY AND CONGENITAL ABNORMALITIES

	Abnormal		*Renal glycosuria*		*"Undiagnosed" glycosuria*		*Control*	
	No.	*%*	*No.*	*%*	*No.*	*%*	*No.*	*%*
Multiple Pregnancy history	2/35	5.7	0	—	3/37	8.1	8/374	2.1
present pregnancy	1/39	2.6	0	—	0	—	5/500	1.0
Congenital Abnormality history	0	—	0	—	1/37	2.7	10/374	2.7
present pregnancy	1/39	2.6	0	—	1/37	2.7	13/500	2.6

Fetal Morbidity and Mortality

In Tables XIV and XV an attempt has been made to compare the immediate condition at birth, the fetal losses and the course of the survivors in the nursery.

TABLE XIV.—APGAR RATING*

APGAR	*Abnormal*		*Renal glycosuria*		*"Undiagnosed" glycosuria*		*Control*	
	No.	*%*	*No.*	*%*	*No.*	*%*	*No.*	*%*
< 5	3	7.3	1	2.2	2	4.4	27	5.3
5 — 7	7	17.1	8	17.4	8	17.8	53	10.5
8 — 10	31	75.6	37	80.4	33	73.3	406	80.4
Abortion	0	—	0	—	1	2.2	10	2.0
Intrauterine death	0	—	0	—	1	2.2	9	1.8
Neonatal death	0	—	0	—	0	—	12	2.4
	41		46		45		505	

*A system for judging the condition of the newborn, applied one minute after birth, based on heart rate, respiratory effort, muscle tone, reflex irritability and colour.

TABLE XV.—AVERAGE WEIGHT LOSS (PERCENT BIRTH WEIGHT)

Weight (lb.)	*Abnormal*		*Renal glycosuria*		*"Undiagnosed" glycosuria*		*Control*	
	No.	*%*	*No.*	*%*	*No.*	*%*	*No.*	*%*
< 5.5	1	1.1	1	6.9	1	4.0	36	6.1
5.5 — 9	28	4.4	37	4.7	39	4.4	400	4.7
9+	11	4.8	8	4.2	3	3.9	39	5.1
Overall	40	4.4	46	4.7	43	4.4	475	4.9

The fallibility of using the APGAR rating[27] as the sole method of comparing immediate condition of infants at birth is appreciated. However, as it does provide an easy and useful method of comparison it has been used here. In the abnormal group 75.6% of the pregnancies resulted in infants with an APGAR rating from eight to ten and 7.3% resulted in infants with a rating below five. In the control group 80.4% of the pregnancies resulted in

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infants with a rating from eight to ten and 5.3% resulted in infants with a rating below five.

There were no fetal losses in the abnormal group in this series despite the fact that labour was artificially induced in only 10% of the group, and 13 of the 41 women in this group (31.7%) were not seen prenatally until after the 36th week of pregnancy. Five (12.2%) in this group were not seen until after the 39th week of pregnancy. Two of the latter five were first seen in labour and had no prenatal care. These findings do not corroborate the 25.6% fetal loss in the group of women seen late in pregnancy reported by Carrington, Shuman and Reardon.[2-4] Since the two most common findings in the abnormal group in most series of prediabetics reported are the tendency to have large babies and the higher incidence of toxemia, the findings suggest that fetal outcome is largely dependent on good obstetric management of the latter two conditions rather than on any direct correlation to the abnormality of the glucose tolerance curve alone.

Weight loss in the nursery has been calculated as a percentage of body weight at birth and has been utilized here in an attempt to indicate the nursery course (Table XV). The majority of the discharge weights are those recorded on the sixth and seventh day, only an occasional weight being taken on the fifth day if the child was discharged at that time. If the child remained in hospital longer than one week for any reason, the weight used was that recorded on the seventh day. The weight loss as a percentage of body weight for premature, average size and large babies in each group is shown in Table XV. For babies in all three weight ranges the average weight loss was no greater in the abnormal group than in the control group, and there was no significant difference in the average weight loss of the babies in any of the groups. In the abnormal group the weight loss was not found to be related to the degree of abnormality of the glucose tolerance curve in the mother as previously defined, based on two-hour blood sugar determinations. The average weight loss in groups I, II and III was found to be 5.5%, 2.9% and 4.6% of birth weight, respectively. This is in agreement with the findings of Farquhar and Sklaroff,[6] who noted that postnatal weight loss was related to the delay in allowing the baby to feed, but was no different in babies of diabetic and non-diabetic mothers.

CONCLUSION

Recognition of the prediabetic syndrome was probably not significant in the favourable fetal outcome in this series since the management of the pregnancy and the delivery was not influenced by the finding of an abnormal glucose tolerance curve that was not frankly diabetic.

At the present time the main value in recognizing the prediabetic syndrome in a pregnant woman is to focus attention on the known associated obstetric complications and on the probability of the onset of frank diabetes during the pregnancy or at a later date.

If it can be shown that the prediabetic state in the mother has a bearing on the onset of diabetes in the offspring, it will become more important to recognize and treat the biochemical abnormality in the mother for the future welfare of the child.

Recognition of the prediabetic state is of practical importance as well as theoretical importance and many of the features associated with this state warrant further investigation.

SUMMARY

The significance of the prediabetic state has been reviewed.

Carbohydrate tolerance in the pregnant and non-pregnant individual has been discussed.

The findings in a group of 610 women seen at the Women's Pavilion of the Winnipeg General Hospital, including 41 women with abnormal oral glucose tolerance curves, have been presented and discussed.

The increased incidence of history of multiple previous fetal losses, and of toxemia, large babies and family history of diabetes reported in the literature is confirmed.

No significant increases in difficulty during labour, fetal abnormalities, fetal loss in present pregnancy or fetal neonatal morbidity were noted in this small series.

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AN EPIDEMIC OF TRIORTHOCRESYLPHOSPHATE POISONING*

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THE INGESTION of a neurotoxin with subsequent paralysis of a large number of persons is not a commonplace event. One epidemic was reported in 1930[1] in which it was estimated that up to 20,000 persons in the southern United States suffered from drinking "ginger jake" with resultant "jake paralysis". The toxic ingredient involved was triorthocresyl phosphate. The same contaminant was responsible for a recent epidemic of poisoning with the resultant paralysis of approximately 10,000 natives of Morocco.

The outbreak occurred around five cities in Morocco following the Feast of the Prophet at the end of August 1959. It affected only Moslems, and only those Moslems who lived in the poorer native quarter of each city. It was their habit to purchase cooking oil from bulk containers. The supply of regular cooking oil (olive) was adulterated by the addition of up to 20% of high-compression engine oil which contained triorthocresylphosphate (T.C.P.)

The presenting complaint of most patients was aching pain and tenderness in the calves, with difficulty in walking and loss of light touch perception in the hands and feet. This sensory disturbance cleared in one to two days and was replaced by motor weakness involving, first, the muscles of dorsiflexion and eversion of the foot and a little later the calf muscles, progressing to inability to stand or walk. Motor weakness of the hands was seen in about 10% of the patients, mostly those in the older age group.

Following ingestion of the oil, about one-third of the patients had nausea and vomiting for 48 hours. After this nausea there was a latent period varying from eight to 35 days before the onset of pain, sensory disturbances and weakness which brought most of the patients to hospital. In about 25% of the cases the paralysis was introduced by a prodromal stage of transient fever of about 38° C., a reappearance of the diarrhea, and a "flu-like" malaise.

When the victim was examined in the hospital, the temperature and cardiac rate were characteristically normal. The patient did not look toxic. The cranial nerves were intact with the exception of loss of light touch over the trigeminal area and a loss of corneal reflex in about 2% of cases. There were no abnormalities of the cerebellar system, no rhombergism and no astereognosis.

Examination of the upper extremities showed a varying picture depending on the severity of the disease. If the lower extremities were severely affected, there was functional loss of the interossei and small muscles of the hands with intact triceps, biceps, and wrist jerks. Sensory changes in the hands or upper extremities were rarely encountered. The abdominal and intercostal areas were spared. In the lower extremities, there was a loss of function of the dorsiflexors and evertors of the foot, to varying degrees. This might be associated with loss of the function of the calf muscles as well. The Achilles tendon reflex was usually abolished; patellar tendon reflex was present. Plantar reflexes were usually not present.

There was usually a diminution of pinprick sensation over spinal segments from which the paralyzed muscles arose. In a few patients loss of temperature sensation was evident.

There were also a few patients who had loss of bladder sphincter control with retention and later incontinence.

Several clinicians noted that hyperactive reflexes, for example in the Achilles tendon, subsequently progressed to abolishment when the peripheral paralysis appeared.

Laboratory tests of peripheral blood and cerebrospinal fluid showed no abnormalities.

The disease affected all age groups. The severity seemed roughly in proportion to the amount of contaminated oil ingested; e.g. the head of the family, who ate only one meal at home per day, was usually less affected than the wife or children. It was also possible to correlate roughly the incidence and severity of spasticity with the amount of neurotoxin ingested. Children usually showed less involvement than adults except for those who were very severely affected. Of 16 gravid women at seven to nine months' gestation, five had premature delivery of babies who showed no signs of peripheral neuropathy.

When the Moroccan Government called upon the International Red Cross for assistance, six treatment centres were organized[2] under the direction of Dr. Gustave Gingras of the Canadian Red Cross to examine, prescribe, and treat these people.

Treatment in the initial stages consisted of exercise therapy and training in the activities of daily living. In addition, several medical regimens were tried, including corticosteroid therapy and vitamin B and vitamin B_{12}. No definite conclusions could be drawn concerning their effects, if any.

Within eight months, 20% of the patients were improved sufficiently to be discharged from treatment or supervision. In a large majority of the remaining cases, recovery was complicated by the appearance or exacerbation of spasticity. It had been noted in a few cases that spasticity persisted from the onset. However, several cases were subsequently observed where the patient had gone through the stages of flaccid paresis to apparent

*The observations reported in this paper are based on a study conducted while the author was in Morocco on assignment for the Canadian Red Cross Society.

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complete recovery, only to develop spasticity of such a degree later that he was severely incapacitated.

This spasticity was not associated with bladder hypertonus or other changes. The same patient might exhibit clonus at the knee and a flaccid paralysis at the ankle. The lesions were not symmetrical. One patient had hyperactive reflexes at the ankle and at the knee on his right side, but these reflexes were absent on the left side.

The sensory changes that were noted in the early stages of the disease were no longer present. Many of the patients complained of pain in the calves which were often tight and presented zones of swelling and tenderness. These zones were about the size of a pigeon's egg and felt firm to the touch. The pain could be relieved by local injection of procaine. This was seen most frequently when the muscles were recovering and especially when they had attained from 2+ to 4+ strength.* It usually disappeared at 5+ strength.

Other common complaints were those of swelling, rubor and burning pain in the feet. The peripheral pulses were present. There was no thickening of the plantar fascia. There was no pain on extension of the metatarsophalangeal joints. It was felt that this pain in the feet was the pain of a "sympathetic dystrophy". Radiographs of the feet showed some demineralization but no bone cysts. Many of the men complained of impotence.

By the end of the first year, it was possible to group recovery into four categories: (1) flaccid paralysis which progressed to partial or complete recovery and discharge of the patient from further care; (2) flaccid paralysis which progressed to spastic paralysis; (3) flaccid paralysis which went on to spastic paralysis in the lower extremities and flaccid paralysis in the upper extremities; (4) flaccid paralysis which persisted as such with severe disability. In the patients who manifested spasticity, spastic deformities occurred.

The majority of patients could move about, using sticks or crutches. Many of those who had some spasticity used their spasticity to assist them in walking. If the spasticity had been relieved by surgical or pharmaceutical methods, they would not have had enough muscle power to stand.

Of the 400 patients at Fez, an in-patient centre where many of the severe cases were collected, approximately 60 had deformities of such a degree that they required surgical correction; 200 required other procedures such as bracing or special shoes; and 60 were permanent hospital patients because of severe disability associated with other illnesses such as tuberculosis or general debility associated with age.

Several different types of braces were used. If there was a slight weakness of the dorsiflexors of the foot, a Khemisset boot, an inner boot lacing from the toes to above the ankle and worn beneath normal shoes, was used. If the paralysis was greater but in balance, i.e., flaccid and correctible, a Heidelberg brace, a cuff with a posterior spring running down the posterior aspect of the leg to a metal foot plate was used. This arrangement had the advantages that it could be changed from one shoe to another and there was no external spring to be fouled by mud or foreign material. Patients with some spasticity and loss of dorsiflexion were provided with an inner boot that had a metal plantar plate and double standard on each side of the leg which led to a joint at the ankle that, in turn, led to a calf cuff. This partially enabled the patient to keep his forefoot up and helped to counteract some of the spasticity.

Twenty younger patients with short Achilles' tendons and minimal spasticity were placed in corrective plaster in an attempt to stretch the tight heel tendons. The casts were left on for four weeks. On removal five showed definite improvement. Plasters were reapplied in five others.

An attempt was made to reduce spasticity in 19 younger patients by injecting absolute alcohol into the Achilles' tendon to reduce or erase proprioceptive impulses. These children lost their ankle clonus and, with the aid of successively shorter lifts under the heels, began to walk. It was too early to estimate the ultimate result at the time of their last assessment.

Twenty spastic patients were treated with zoxazolamine in a dose of 3 g. per day. Changes in spasticity were measured by the response to a standard patellar tap and by decrease in the size of the zone from which hyperreflexic action could be elicited. There was no evidence of any decrease of spacticity by these criteria.

The operative treatment proposed for those patients with fixed equinus deformities consisted of elongation of the Achilles' tendon with or without posterior capsulotomy. For postural flexion deformities of the knee, Eggers' procedure was recommended. Tendon transplantation was largely a theoretical consideration because most of the patients objected to anesthesia and surgery and it was felt that if external bracing could permit them to become mobile, it was the treatment of choice.

Patients recover from flaccid paralyses at a rate similar to that proposed by Sharrad for plotting the recovery of patients with poliomyelitis. The speed of recovery was usually related to the age of the patient; for example, for the gastrocnemius it required an average of eight months to improve from 0 to 2+ or 3+ strength in patients under 25 years of age and 10 months in those over 25. For those with gastrocnemius strength of 3+, the time which elapsed before the small muscles of the foot showed 2+ to 3+ strength, was seven weeks for patients under 25 years of age, and 11 weeks for those over 25 years.

*The International Scale for grading muscle strength is charted on a numerical basis. A normal muscle is graded 5, a muscle which can just lift a limb against gravity is 3, a muscle with a flicker of movement on tensing is graded as 1, and muscle in which there is no actvity is graded 0.

Extreme flaccidity was commonly associated with a relaxation of articular ligaments with a resultant hypermobility of the affected joints. It was difficult to determine whether this was due to a true ligamentous relaxation or to too early and vigorous walking without support.

In 40 spastic patients who complained of knee pain and were studied radiographically, two showed radiological evidence of osteochondritis dissecans which was bilateral in one case.

Eighteen months after the onset of the disease process, it is still too early to determine how many patients will be permanently incapacitated. According to estimates by Weber[3] during the discussion of poisoning by Jamaica ginger, 25% of people seen in the follow-up study were still incapacitated four to six years later. In the cases of the Moroccan epidemic of paralysis it will be very difficult to arrive at a true estimation of the extent of permanent disability as many of the victims have disappeared into the hills and will not be seen again by medical personnel.

This epidemic of triorthocresylphosphate poisoning has differed in certain features from the major epidemic in the United States in 1930. In the latter there was a higher percentage of abdominal and lumbar involvement with some deaths due to respiratory failure; and sensory changes, which were present from the first, persisted in several cases.

Because of religious beliefs involved, it is not possible to obtain adequate postmortem examinations of the Moroccan patients. One or two muscle biopsies showed patchy fibrosis with nerve changes compatible with those of a peripheral neuropathy. In the reports of these biopsies, there was no mention of the changes, thickening of all the coats, and a narrowing of the lumen[4] which have been described previously in the small arteries, particularly capillaries and pre-capillaries in these cases.

Because of the mode of onset in this disease, it is necessary to explain the appearance of spasticity at a late date. If the changes described previously in the spinal cord in T.C.P. poisoning,[4] namely those of thickening of the walls of the small spinal arteries with some thrombosis of capillaries, could be postulated in this outbreak, it is possible that fibrotic changes occur in the spinal cord on an ischemic basis leading to late spasticity. Such spasticity, because it is secondary to an ischemic process, would take longer to appear than the flaccidity caused by the action of a peripheral neurotoxin.

SUMMARY

Approximately 10,000 members of the Moslem population of Morocco were poisoned by cooking oil contaminated by triorthocresylphosphate, with subsequent development of varying degrees of paralysis.

Approximately 25% have recovered, 50% are still recovering or have been fitted with braces to aid in their rehabilitation to the level of self-employment, and 25% have spasticity or general debility to such an extent that they will be permanently incapacitated.

The appearance of spasticity one year after ingestion of the oil, and sometimes after apparent recovery from flaccid paralysis, is described.

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LYMPHOSARCOMA OF THE APPENDIX

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LYMPHOSARCOMA of the appendix is uncommon and few patients with this lesion survive more than two years. In the stomach and intestine, lymphosarcoma is a well-known lesion. It may also occur in the tonsils, lymph nodes, spleen and thymus gland, and more rarely in the lymph follicles of the gastrointestinal tract. Geschickter[1] reported that sarcoma, mainly in the form of lymphosarcoma, comprised 3% of all malignant tumours of the gastrointestinal tract. In his series of 46 lymphosarcomas of the gastrointestinal tract none were found in the appendix. Usher and Dixon[2] reviewed 50 cases of lymphosarcoma of the intestinal tract seen at the Mayo Clinic and reported none in the appendix. Ullman and Abeshouse[3] compiled 126 cases of lymphosarcoma from the literature and found only two involving the appendix and one that involved both the cecum and the appendix. In 1939, Ewing[4] described two types of sarcoma arising in lymphoid tissue, a malignant lymphocytoma and a reticulum-cell sarcoma. He pointed out that lymphoid tissue contained three main cellular elements, lymphocytes, reticulum cells of the pulp and follicles, and endothelial cells of the pulp and sinuses. Clarke and Simonds[5] collected 20 cases of the lymphocytic or reticulum-cell type and 11 cases of giant follicular lymphoblastoma of the appendix. The lymphocytic type is more malignant and tends to occur at an earlier age than the giant follicular lymphoblastoma.

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CASE REPORT

A 17-year-old man was admitted to the Toronto Western Hospital on July 31, 1953. He gave a history

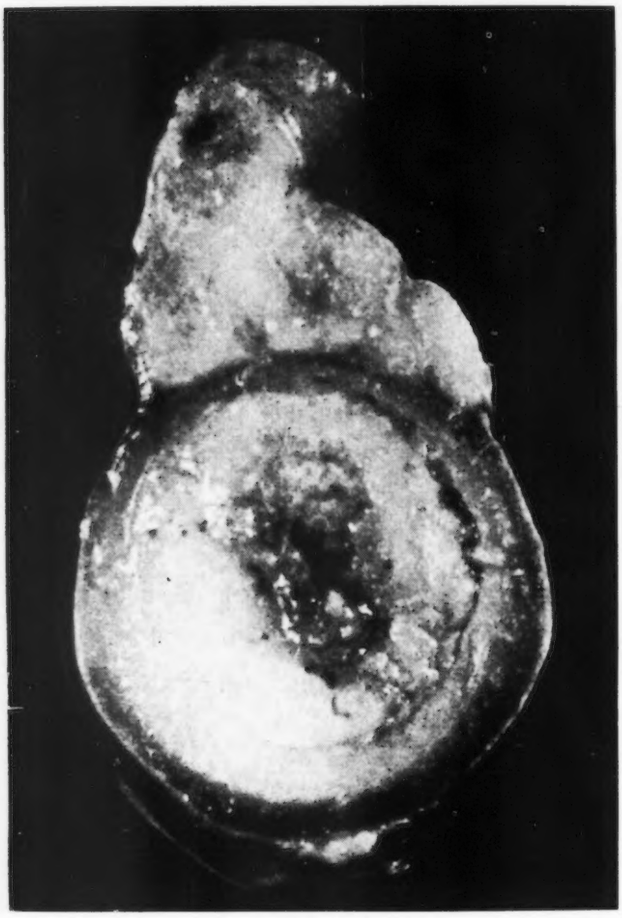

Fig. 1.—Gross section through the distal portion of the appendix, showing the tumour.

of epigastric pain which occurred on July 30, 1953. He had been awakened at 4 a.m. on July 31 with severe, right lower quadrant abdominal pain, and became nauseated and vomited at 8 a.m. on the same day. On examination, his temperature was 101° F., his pulse was 102 per minute and his white blood count was 17,800 per c.mm. The abdomen was flat, with marked tenderness in the right lower quadrant. Rectal examination revealed tenderness high on the right side, but no masses were felt.

An appendectomy was carried out at noon on July 31. The appendix appeared acutely inflamed and measured 9 cm. in length and up to 2.5 cm. in diameter. The external surface was hemorrhagic and edematous, ranging in colour from bright red to purplish black. There was a filmy, yellowish-green exudate on the serosal surface. On cross section of the appendix, the proximal portion was of normal diameter. The distal half of the appendix was extremely edematous, soft, boggy and yellowish-white in colour (Fig. 1). There was a small fecalith in the lumen of the most distal portion, and the contents of the lumen in this region appeared to be in the nature of purulent exudate.

Microscopic examination of the proximal portion of the appendix showed a patchy ulceration of the mucosa with acute inflammatory cell infiltration and edema involving all layers of the wall, including the serosa and mesoappendix. Sections from the thickened distal portion of the appendix showed a tumour which involved the entire submucosa and compressed the lumen (Fig. 2). This tumour infiltrated the muscularis mucosae and at one point extended for a short distance into the mesoappendix. It was seen to consist of sheets of lymphatic cells which showed no tendency to form germinal follicles. The mucosa had been replaced almost entirely by tumour, and only a few isolated glands remained within the lymphoid stroma (Fig. 3). The tumour did not involve the serosal surface, and the cells did not produce reticulin. The pathological diagnosis was acute suppurative appendicitis and fecalith of the appendix, and lymphosarcoma of the appendix (lymphoblastic type).

On August 10, 1953, ten days after the appendectomy, a right hemicolectomy was carried out. There were several enlarged lymph nodes in the ileocecal region which on pathological examination were found to exhibit acute catarrhal lymphadenitis. No tumour was found in the lymph nodes or in the terminal ileum and ascending colon which had been removed.

The patient made a satisfactory recovery and was discharged from the Toronto Western Hospital on August 24, 1953. He remained well until November 6, 1953, when he developed steady, severe pain in the right lower quadrant and was readmitted for three days, at which time a provisional diagnosis of renal colic was made. Following this episode, the patient was well until June 1956, when he developed pain in his left upper quadrant, following the lifting of a heavy weight. On examination the tip of the spleen

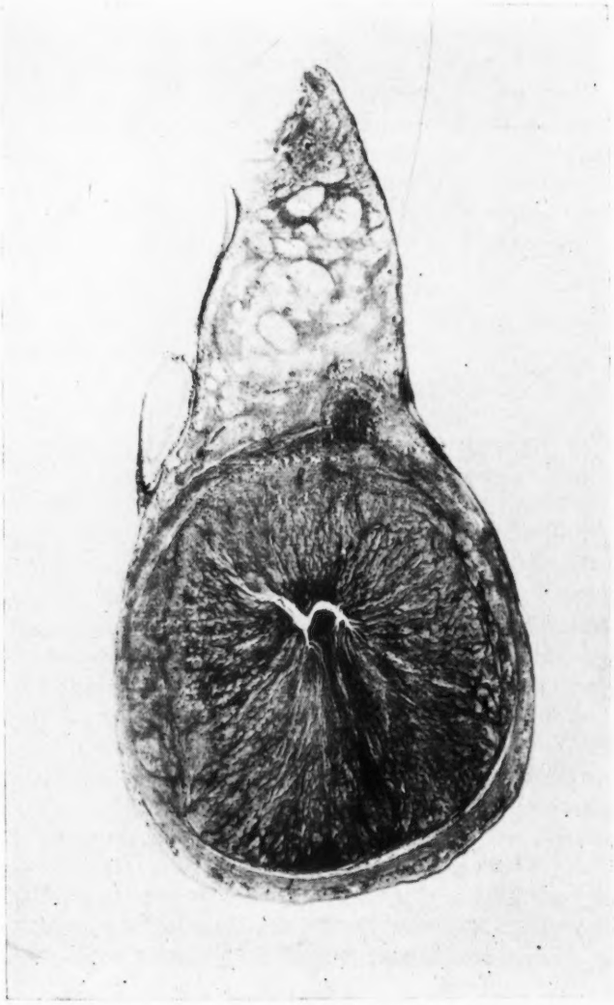

Fig. 2.—Photomicrograph of distal portion of the appendix showing the tumour replacing the mucosa and submucosa. The tumour is seen penetrating into the mesoappendix at one point. (Reticulin stain, ×4.)

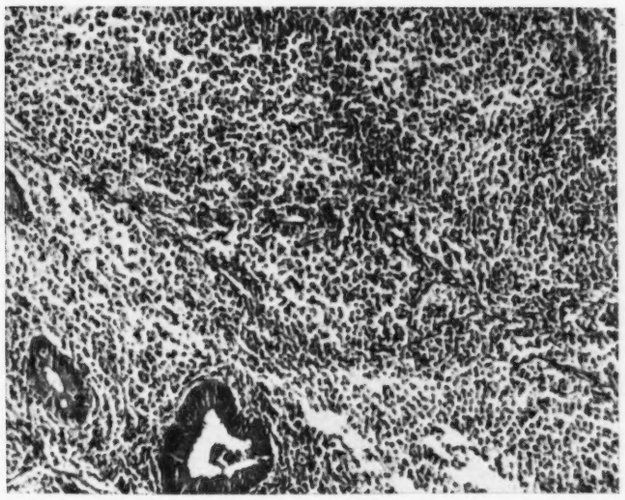

Fig. 3.—Photomicrograph of the appendix showing replacement of the mucosa by tumour tissue. A few isolated mucosal glands are seen in the section. (H & E, x 150.)

was palpable, but no lymphadenopathy was found. The hemogram at that time was normal.

On April 22, 1957, the liver was found to be enlarged two fingerbreadths below the costal margin and the spleen was three fingerbreadths below the costal margin. These findings suggested a spread of lymphosarcoma, but the hemogram was normal and no treatment was given. The patient was examined at six-month intervals thereafter, and the findings regarding the liver and spleen remained unchanged. The hemogram on December 19, 1960, revealed a hemoglobin of 16.3 g. %, a white blood count 10,950 per c.mm. and a sedimentation rate of 1 mm. per hour. The blood smear showed slight anisocytosis, the platelets were abundant, and the differential leukocyte count was as follows: neutrophils 62%, eosinophils 1%, lymphocytes 21%, monocytes 13%, neutrophil myelocytes 1%, plasma cells 1%, and Turk cells 1%. During the past two years this young man has worked steadily as a service station operator and, on his most recent examination on June 10, 1961, he appeared in excellent health, with no symptoms and no changes in his physical findings, the liver and spleen remaining palpable.

DISCUSSION

In lymphosarcoma of the appendix, the glandular pattern of the mucosa is obscured or even replaced by the proliferating tumour cells. Clinically, the diagnosis of appendicitis, either acute or chronic, is generally made but the diagnosis of lymphosarcoma is usually established only on pathological examination.

A review of the literature by Knox[6] revealed 17 instances of lymphosarcomas of the appendix. Clarke and Simonds[5] reported a single case in 1951, and a further case was reported by Henley and Slack[7] in 1954. The patients' ages ranged from 4 years to 45 years. The survival time was approximately seven months, and three years was the longest period of freedom from recurrence.

The interesting feature in the case described in this report is the evidence of acute appendicitis in the proximal portion of the appendix, the tumour being located in the distal segment.

The treatment of lymphosarcoma of the appendix is usually appendectomy, occasionally followed by radiotherapy. A right hemicolectomy has also been advocated and was carried out, in the case reported, ten days after appendectomy. Clarke and Simonds pointed out that lymphosarcoma of the appendix is less frequently associated with acute appendicitis and perforation than is true carcinoma of this organ. Thus, operation may be resorted to later in the disease.

SUMMARY

A case of lymphosarcoma of the appendix (lymphoblastic type) is reported. To date, the patient has survived eight years since the diagnosis was established. The treatment in this case was primary appendectomy for acute appendicitis and ten days later a right hemicolectomy.

Lymphosarcoma of the appendix is rare, in spite of the fact that the appendix in early life contains relatively greater amounts of lymphoid tissue than any other part of the gastrointestinal tract. The prognosis is poor and the average survival is seven months. The longest period of freedom from recurrence previously reported was three years.

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PAGES OUT OF THE PAST: FROM THE JOURNAL OF FIFTY YEARS AGO

RESUSCITATION BY CARDIAC MASSAGE

The power of the heart to resume its function is well known to laboratory workers. Cardiac massage, although suggested by Schliff in 1874, was not applied to man until 1898. The primary essential is the presence of sufficient pressure in the ventricles and coronary arteries. In animals this maybe obtained by injecting saline solution into the superficial veins, but this method has not been applied with equal success to the human subject. When, for some reason or another, the action of the heart in man has been arrested, there remains but one practical method of resuscitation, namely, cardiac massage. In a series of forty-six cases collected by Cockovic, the method was successful in restoring the cardiac rhythm permanently in twenty per cent. of the cases.

Three methods have been employed: (1) direct, (2) trans-diaphragmatic, (3) subdiaphragmatic; the latter having yielded the best results.—C. H. Frazer in the *Journal of the American Medical Association;* abstracted in the *Canad. M. A. J.*, 1: 909, 1911.

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Sept. 16, 1961, vol. 85

SPECIAL ARTICLE

HOME PHYSIOTHERAPY FOR ARTHRITIC PATIENTS IN RURAL SASKATCHEWAN: A PROGRAM OF THE CANADIAN ARTHRITIS AND RHEUMATISM SOCIETY (SASKATCHEWAN DIVISION)

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INTRODUCTION

AT ITS Annual Meeting in January 1958, the Medical Advisory Committee of the Saskatchewan Division of the Canadian Arthritis and Rheumatism Society (C.A.R.S.) re-examined the existing physiotherapy program of the Society. This constitutes only a portion of the total program of the Division, which includes maintenance of beds in two hospitals for treatment and research, provision of equipment to physiotherapy departments in regional hospitals, scholarships for physiotherapy students, provision of educational material to doctors and to the lay public, and donations to the research funds of the national office of C.A.R.S. A closely allied service has been the establishment and continuation of medical consultative clinics throughout the province. To these clinics, which have been in continuous operation since 1949, come patients referred by their family physicians. Advice concerning the total care of the patient is given to the physician by the consultant. If physiotherapy is recommended, the family physician may ask the therapist to carry out the prescribed treatments. The family physician has also been at liberty to refer the patient directly to the therapist without making use of the consultative clinic. The therapist, who is a member of the Canadian Physiotherapy Association and of the Saskatchewan Physical Therapists Association, sees only those patients who have been referred in either of these two ways.

In order to carry out the treatments, the therapist has been provided with a vehicle equipped with shortwave machines, infra-red lamps, wax baths and similar equipment. Two groups of patients received these benefits: (1) homebound patients suffering from rheumatic diseases and living in the urban areas of Regina and Saskatoon; and (2) those who could attend clinics in rural areas served by mobile physiotherapy units. One drawback to this type of therapy was that it mitigated against the patient taking an active role in his own treatment. It is unreasonable to expect improvement in a clinic situation when the patient travels a long distance once a week, receives a wax bath or twenty minutes of diathermy followed by a few exercises and then returns home with little or no instruction on continuation of these exercises.

Besides this, another important defect in this program was the feeling, experienced by the physiotherapist, of relative isolation from her colleagues. She found it difficult to obtain adequate supervision or recognition for her work, either from medical practitioners or from other physiotherapists. She had no one with whom she could discuss problem cases. Very few complete prescriptions for therapy were given to her, and she frequently had to write her own. She had to evaluate the results of treatment and decide how long it should be continued. Many of these therapists have felt that the good hours, higher rates of pay and numerous fringe benefits which the Society provides do not compensate for these deficiencies and have elected not to remain with the Division.

With these disadvantages in mind, the Committee drew up a plan in which the patient would take a much more active role. The therapist would visit the patient in her home, carry out a rapid assessment of her functional limitations and recommend changes in furniture, bathroom facilities, height of bed, softness of mattress, and the like. She might prescribe exercises which she could teach the patient in such a way that their performance would be continued without supervision. On her next visit, she could report progress to the family doctor and get his suggestions and co-operation regarding further methods of improving the patient's activities of daily living and general functional capacity.

A program like this had not been launched earlier because of the apparent impossibility of serving a scattered rural population which was relatively isolated either by snow or mud for over six months of each year. Accordingly, the Saskatchewan Division planned a project for a small area of the province which was to be evaluated after one year and subsequent action decided upon. The cost was well within the budget of the Society, since no new equipment or physiotherapy staff was needed. As in its total program, the funds were provided entirely by the people of Saskatchewan. The project began on May 1, 1958, and was carried out during its first year of operation by one of us (R.H.F.)

METHOD

The area chosen for this project was a rectangle at the southeastern corner of Saskatchewan, roughly 150 miles long and 100 miles wide (Fig. 1). It is

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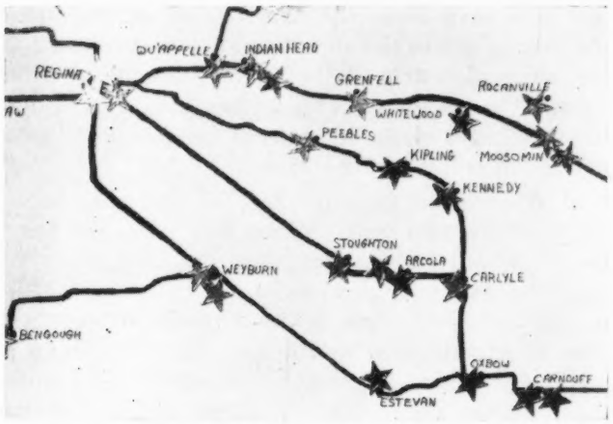

Fig. 1.—Regina and the surrounding rural region which is 150 miles east-west and 100 miles north-south. Stars give location of clinics.

served by four main highways fanning out to the east and south from the city of Regina, located at the northwest corner. Two of the four highways, the Trans-Canada running east for 150 miles to the Manitoba border, and the most westerly, running south and southeast through Weyburn and Estevan to the international boundary, are paved. The other two main routes are good gravel roads but the communicating sideroads become largely impassable, both in winter and in the spring, when the snow is replaced by mud. Topographically the region is prairie, interspersed with rolling hills and wooded areas. The main occupation in the area is farming. Excluding Regina, the largest community is Weyburn, with a population of approximately 8500. Most towns in the area have a population of about 1000 but the majority of people live on relatively isolated farms or in small communities.

Besides the obvious difficulties involved in driving long distances under severe weather conditions, the Medical Advisory Committee of the Saskatchewan Division wanted to know whether the proposed forms of treatment, which completely discarded the "heat and massage" type of supportive therapy, would be accepted by the doctors and their patients. They also wished to determine whether the smaller number of patients treated would justify the cost involved.

Initially, this program was to have been entirely a home-treatment service. It soon became apparent that, although most of the available time would be spent doing home visits, it would be advisable to have a few regular half-day clinics in main centres. These clinics would reduce the amount of the physiotherapist's time spent in travelling, would enable local doctors and new patients to contact the therapist more easily each month, and in certain cases some patients would benefit by attending a formal clinic by leaving the home and its distractions behind them for a short period. The therapist could follow up the clinic patients by visiting their homes; construct devices to assist them in the performance of appropriate exercises; and make plaster splints, and so forth. These clinics were located at the points indicated by the stars on the map (Fig. 1).

The therapist was able to reach all communities in the designated area. When isolated farms became inaccessible to ordinary travel during extreme weather conditions, the patients came to the clinic, using heavy farm equipment as their mode of travel. The services were never suspended and in the 12-month period the therapist travelled 22,916 miles.

The home treatments were active, not palliative, since the aim of the service was to assist the patient to become as self-sufficient as possible. Simple, homemade, adaptive apparatus was frequently used. For example, the therapist would arrange with the family to set up auto-assisted pulleys over door frames or would devise spring-resistance devices utilizing door springs or old inner tubes. She always carried strips of car or bicycle tire tubes, a finger exercise board, a slide board, paraffin wax, a simple neck traction apparatus, plaster-of-Paris, stockinette, Kramer wire and sand (Fig. 2). Many

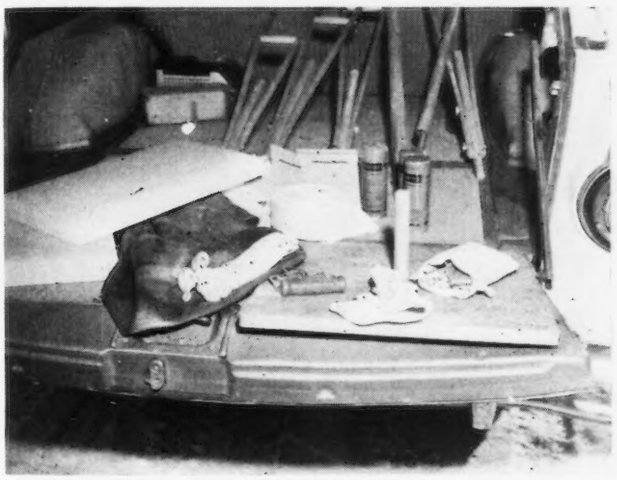

Fig. 2.—Types of assistive apparatus carried in mobile physiotherapy unit.

plaster-of-Paris night splints were made similar to that shown in Fig. 3.

Fig. 3. — The physiotherapist makes splints, etc., from plaster-of-Paris.

Fig. 4.—A slide board with sling resistance provided by strips of inner tube.

The patient in Fig. 4 is using a homemade slide board for hip and knee extension. Initially she used this device alone, but as her muscles became stronger a strip of inner tubing was arranged to act as a resistance; the heel resting on the board helped to guide the direction of the movement. A second wider strip of tubing was later used to increase the resistance. This patient also does abduction exercises of the hip by placing the board sideways across the foot of the bed.

Fig. 5.—An auto-assisted pulley exercise. The pulley can be attached to a door frame. Note large hand-grip to accommodate hand deformity.

A 63-year-old patient (Fig. 5) had rheumatoid arthritis for two years. When first seen, her knees were painful and swollen; her shoulders were stiff and there was limitation of all movements. Her hands had some ulnar deviation and movements of the interphalangeal joints were limited. She was given quadriceps exercises with excellent improvement in the knees. The shoulders remain stiff and at the last reported visit she was fitted with the pulley and rope device as illustrated. This apparatus could be fastened to a door frame or cupboard or other convenient projection.

The patients were often skeptical that a "do-it-yourself" program would help their condition, particularly when they had previously received passive treatment either in hospital or in mobile clinics. The previous methods had given more immediate comfort but the results were shortlived. Under the present program, exercises had to be interesting, as well as simple and effective, before the patients would continue to carry them out for a whole month without supervision. The therapist often spent time working out solutions to the small but frustrating problems with which the disabled homemaker has to contend. Her work inevitably overlapped the fields of occupational therapy, nursing and social case work. The public health nurse was a valuable ally when the family found that special help was needed. Good neighbours were the rule and willingly assisted in constructing many of the simple devices that were required. The therapist was able to maintain excellent relations with the family doctors involved and towards the end of the year the number of referrals was showing a steady increase.

RESULTS

Because of the long distances and the perennial shortage of physiotherapists, the therapist often treated non-arthritic patients. The total number of patients with "arthritis and allied conditions" treated during the 12-month period is shown in Table I.

TABLE I.

Rheumatoid arthritis	48
Marie-Strümpell spondylitis	1
Arthritis due to trauma	1
Degenerative joint disease	46
Non-articular "rheumatism"	5
"Bursitis", periarthritis, etc.	10
	111

Table II shows the remaining caseload.

TABLE II.

Cerebrovascular diseases	7
Cerebral palsy	4
Poliomyelitis	3
Miscellaneous neurological disorders	5
Backache (unspecified)	2
Miscellaneous orthopedic disabilities	23
Miscellaneous medical conditions	4
	48

Treatment was terminated in 79 of the 159 cases during the year, as indicated in Tables III and IV.

TABLE III.

Response	*Rheumatic patients*	*Non-rheumatic patients*
Improved	36	21
Unimproved	16	6

TABLE IV.

Reason for termination	*Rheumatic patients*	*Non-rheumatic patients*
Maximum benefit	33	19
Non-cooperation	16	3
Other	3	5

(N.B.—"Non-cooperation" includes those cases in which the therapist considered that there was insufficient co-operation to justify continuation of visits involving such long journeys.)

DISCUSSION

It is not possible to make an analysis of these results in terms of improvement in the disease. Improvement can be judged to have occurred if the patient's activities of daily living have increased in scope or in the ease with which they are accomplished. The cases designated "unimproved" include the 19 in which treatment was terminated because of "non-cooperation". Subjecting such figures to statistical methods would be meaningless.

Since the completion of the original investigation in April 1959, the work has been carried on by two other therapists. The steady increase in referrals, to the point where the present therapist felt unable to cope with the caseload and asked for assistance, is an indication of its popularity with both doctors and patients.

The cost per treatment varied from month to month. By adding the mileage costs (10c per mile) to the monthly salary of the therapist and dividing this amount by the number of treatments, the cost was estimated at $6.00 per treatment as compared with $1.10 for that provided by another therapist who serves two urban centres, 30 miles apart. At present, the cost per treatment has dropped to $3.40 in the rural area and has risen to $1.60 in the urban centres.

Because of the relatively large distances involved, fewer patients are treated each day. These patients are seen approximately once per month and are so instructed that they will conduct their own treatments with the help of their families during the intervening time. The overall effect is that the patients receive more treatment, although they see the therapist less often.

The success of a program like this is dependent upon its physiotherapist. Primarily, she must be adequately trained in a recognized school and have a year of postgraduate work in a properly directed physiotherapy department of a general hospital.

Some schools of physiotherapy lay more stress on the value of improvisation than do others. The Saskatchewan Division of C.A.R.S. has found that graduates from such schools undertake a project like this more readily than those trained to handle patients in hospital settings. The therapist must be physically strong and in excellent general health. She should be capable of making an accurate clinical appraisal and of taking appropriate action, rather than simply seeing a patient in terms of joint disease alone. She must also be capable of accurately instructing the patient and the family in the performance of the prescribed exercises and of motivating them to continue this program without supervision for relatively long periods. With all of this, the therapist must be able to drive a car long distances without fatigue. Individuals with such qualifications are hard to find and difficult to retain.

SUMMARY AND CONCLUSIONS

A program of physiotherapy is described which stresses means of increasing the activities of daily living for the arthritic patient. Methods used include instruction in active and active-resisted exercises. These are simple but an attempt is made to make them imaginative and interesting, making use of rope, rubber tubing, pulleys and similar equipment. Alterations in home furnishings are recommended, which can be carried out by members of the patient's family. These suggestions include changes in heights of tables and bed, strengthening of stair railings, alterations to chairs and toilets. Although accurate statistical evaluation cannot be made of the results, it was the therapist's clinical impression that improvement in functional capacity had occurred in the majority of cases. It is the opinion of the Medical Advisory Committee of the Saskatchewan Division of the Canadian Arthritis and Rheumatism Society that this type of service is of greater value to its patients than the more conventional methods of physiotherapy and that such service should be expanded. While the cost per visit is roughly double that of an urban program, it is felt that the services rendered by the therapist to the patient and his family justify this expense.

The success of such a program depends in large measure on the experience and resourcefulness of the therapist. She should have at least one year's postgraduate training under adequate supervision in a general hospital and, in addition, a period of orientation in a home-care program before being permitted to accept the responsibility of this type of employment. She should have an adequate opportunity to discuss her work freely with medical practitioners, consultant rheumatologists, a supervising physiotherapist and her confrères. Expansion of programs such as this will depend upon a continuing supply of competent, imaginative graduates from schools of physiotherapy in Canada.

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VIEWPOINTS

WHAT IS A PROFESSION?*

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DEFINITIONS

THE SHORTER Oxford English Dictionary lists no less than seven distinct meanings for the word "profession", while H. W. Fowler does not tackle the problem at all. From the "oldest profession in the world" down to some more modern uses—such as exemplified by "sanitary engineer" for plumber, "mortician" for undertaker and "orbital tactician" for professional football player—the word has lost any claim to precision. Even a legal definition is not much more helpful. It reads as follows: "A profession is a self-selected, self-disciplined group of individuals who hold themselves out to the public as possessing a special skill derived from education and training and who are prepared to exercise that skill primarily in the interests of others."[1] One may be forgiven for seeking refuge with C. L. Dodgson (Lewis Carroll) when in the words of Humpty-Dumpty he said: "When *I* use a word it means precisely what *I* choose it to mean, nothing more, nor less."

HISTORICAL

In early days there were three so-called learned professions: divinity, law and medicine. Their origins arose from a need for individuals, acceptable by the community, as competent to administer the spiritual and corporal needs of the individual and to legalize and regulate the disposal of his worldly goods. It is an interesting and sobering reflection on human values and attitudes that, to the present day in many parts of the world, pure educators, although charged with the responsibility of the basic education for the three traditional professions, are denied public acceptance of their existence as a professional entity with distinctive rights and privileges. Historically, teachers themselves were members of one of the three learned professions and acquired their status through this preparation rather than by any separate identity. There is no doubt that the public school system, with its emphasis on state employment, has retarded to some extent the organization of educators into a separate and distinct profession.

What then constituted a profession in the original historical meaning? Here it is important to note that the earliest universities were founded primarily to prepare students for the professions. This objective has continued to constitute the fundamental relationship between the universities and professional bodies. On the few occasions in history when the traditional ties between a profession and university preparation has waned, the profession has fallen to a very low level. At the turn of this century, doctors in the United States were turned out by so-called "diploma mills", centres not associated with an accredited university. Until the Flexner Commission corrected this state of affairs the standards of medical practice and professional conduct in the United States were at their lowest ebb.

Secondly, the university was responsible for the education of a candidate *prior to* his acceptance for professional training. Is it too much to ask that a primary and essential prerequisite to professional training should be a liberal arts education in a university? If there is one thing that ought to separate the professional area from those areas that are not, it is on the basis of education in its broadest terms, on a knowledge of the cultural streams of our Western society and on an understanding of the relation of man to his environment.

Additionally, in the context of the early days of professionalism, one had to show evidence of being a "gentleman" as well as a "scholar" before being allowed into a profession. A "gentleman" in the historic sense meant a person of gentle birth; one could only be born a "gentleman" but in addition there were assumed qualities of good moral character. Few can regret that the restriction of birth, placed on the word gentleman, has passed away. There is still, however, the implication of standards of acceptable morality and character expected from members of a profession. The supervision of this area represents one of the important duties of a professional organization.

"Scholarship", although changed in curricular content and narrowed by the avid demands of specialization toward technical material, is still observed by required attendance at a university prior to formal professional training. Recently, in view of the growing length of professional courses, there have been demands to abridge even further this period of scholarship. Apart from the goal of excellence that is the common basis of every profession worthy of the name, there is another serious reason, important to society, why standards of university scholarship, with emphasis on the humanities, must be retained as a preliminary to professional training. Schumpeter[2] states, "All those who are unemployed, or unsatisfactorily employed or unemployable, drift into vocations in which standards are least definite or in which aptitudes and acquirements of an indifferent order count . . . They enter these vocations in a thoroughly dis-

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contented frame of mind. Discontent breeds resentment." It is partly for this reason that the requirements for admission to any professional group should be definite and definable, not vague and diffuse.

In this brief account of the origin of the professions, the basic, indeed essential element is established, namely conception and birth within a university. A profession inherits the ideas and ideals of a university: scholarship and research with the single aim of excellence. Without this idealism born in a university, a profession cannot begin to exist.

Legal Status

The second basic essential of a profession is legal status. A profession must acquire a statutory basis in the law of the country. In effect, there is thus created a mutual exchange of definable values between the state and the professional group. For the profession to exist as a recognizable group it is mandatory that the public grant to the professional body, by legislative statute, more or less tangible monopolies, along with self-governing privileges. By statute a professional group is granted the exclusive right of performance in a specific field, be it the practice of law, medicine or engineering. Along with this goes the right to determine its own fee structure or its salary levels. It is of course assumed that this right will be exercised by the professional group with discretion and always with the implied condition that no one shall be denied essential professional service for any reason. Not for reasons of race, creed, religion or ability to pay can needed professional service be refused without laying oneself open to a charge of non-professional conduct. It is with this important qualification that the right of self-determination of the fee structure exists. That this right is sometimes abridged by governmental or private agencies is due to weakness within the professional organization.

In return for this monopolistic right of practice and pay, enjoyed by professions, there is a reciprocal commitment to admit to its circle only individuals of proved competence, to guarantee their trustworthiness, to insist on the observance of an ethical code of conduct, and to protect the public against bungling and extortion.

No profession can exist without this protection under the law. It alone must have the right to set conditions of entrance. It alone must have the right to set codes of professional conduct. It alone must have the right to determine the values of professional competency. It follows from this that it alone must exercise discipline over its members and, with due regard to basic human rights, remove delinquents from its lists. Doctors are stricken from the rolls, lawyers disbarred, priests defrocked.

Let no one underestimate the weight and gravity of this disciplinary power. It takes little account of contemporary standards of work hours, of limits of fatigue, of expectations of monetary compensation, in its stern view of professional duty. There are hard-won and creditable gains accomplished by the growth of the trade union movement in ameliorating and raising the standards of living of the labouring man and of the craftsman. These gains have had no effect on the meaning of professional duty. One can be as guilty of the professional crime of abandonment of a patient at three o'clock in the morning as at ten. The forty-hour week, fatigue, and non-payment of fee weigh nothing as a defence in the professional judgment of this offence. Occasionally, in professional circles, an envious eye is turned to the gains toward a life of regular hours with regular pay achieved by unions by collective bargaining. But never have these achievements become serious considerations in the goals of a profession.

THE GOVERNMENT OF A PROFESSION

The internal government of a profession must lie with its own membership and it must be on the broadest possible democratic basis. No profession can continue to exist if its internal control falls into the hands of government appointees or party representatives. The power of a professional body is great; it includes the denial of entrance and, in extreme cases, the power of expulsion. This is a power too great to be entrusted to the hands of a bureaucracy. It is the duty of government to see that this power is not abused but is used wisely and fairly in the interests of society. But in democratic society, it is not within the right of government to exercise this power by itself.

REMUNERATION

What should be the price that society, either collectively or individually, should pay for a professional service?

Historically, the professional received not a salary nor a fee but an honorarium. Until early in this century doctors in England did not submit a statement of fees but were paid by their patients on a voluntary basis that reflected the financial status of the patient rather than the service rendered. And today in spite of the generality of the "fee-for-service" basis of professional claims, there is a tacit understanding that neither the quality nor the essential quantity of the service is limited by the size of the fee. The honorarium has almost completely disappeared. In all the professions, including the medical, substantial numbers have departed from the traditional "fee-for-service" basis to a straight annual salary. There are many in the professions who deplore this trend as an indication of the degradation of professional status to that of a craft, with the comment that "we are becoming just another bunch of employees".

So long as the professional association remains strong, so long as its standards are upheld, so long as entrance into it is controlled by the professional

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body and by none other, and so long as the association commands respect from the general community, these fears appear to be groundless. Of greater importance than the technique of remuneration, whether by fee or salary, is this essential condition: That the motivation of service to society, the hallmark of a true profession, should be properly rewarded. "We must recognize that one important factor in the unwillingness of youth to undertake certain critical tasks is due to a rather severe imbalance in our current system of incentives. The skills that we need most critically today are not those we reward most highly."[3] Today we are worried about increasing failure in attracting prospective doctors and, more particularly, educators to these vitally important fields. Our scale of material and social rewards and incentives reflects an attitude in which these fields are not accorded a very high priority. If teachers today and doctors tomorrow are not adequately paid, it is at least in part because society still fails to evaluate essential social contributions on a scale comparable to business gain. In the affluent society of John Galbraith, with its areas of "private wealth and public squalor", too often has dedication to society resulted in personal sacrifice. But the correctives for this state are not by the methods of remuneration, be it fee or salary, but by the maintenance of high professional standards and strong professional organizations.

THE SPIRIT OF A PROFESSION

And finally, having been sired by a university and given corporate structure by the law of the land, what is it that breathes life into a profession, gives it character, personality, spirit and soul?

One can take as a text this line from the Sermon on the Mount, "Whosoever shall compel thee to go one mile—go with him twain." Professor Wickenden, speaking before the Engineering Institute of Canada, had this to say:

"Every calling has its mile of compulsion, its daily round of tasks and duties, its standard of honest craftsmanship, its code of man-to-man relations, which one must cover if he is to survive. Beyond this lies the mile of voluntary effort, where men strive for excellence, give unrequited service to the good, and seek to invest their words with a wide and enduring significance. It is only in this second mile that a calling may attain to the dignity and the distinction of a profession."

Herein exists the area of the conscience of the individual member of a profession, his own personal and private sense of dedication to society. It is in this subtle area of private endeavour that a profession, in its totality, achieves greatness. Sometimes it is called professional spirit. It is the result of the association of men and women of superior type with a common ideal of service above gain, excellence above quality, self-expression beyond pecuniary motive and loyalty to a professional code above individual advantage.

Furthermore, no professional man can evade the obligation to contribute to the advancement of his group. His own knowledge is part of a common fund, built up over the centuries, an inheritance which he freely shares but to which he is obligated to add. Hence the duty to publish freely the fruits of his research and to share any advances in professional technique.

THE PROFESSIONS AND HUMAN PROGRESS

Aside from service in specific areas of society's needs, have professions any other value? Do they represent any significant position in humanity's tortured climb, and do they point to any area of hope in a troubled world?

Democratic so-called free societies are faced with a great dilemma: either to become increasingly socialized with an inevitable restriction of personal freedom; or to go back to nineteenth century laissez-faire, with emphasis on unrestricted personal freedom, and a reluctance to enter the sphere of social planning. The extremes of these divergent paths are intolerable to many of us, rooted as we are in the Hellenic philosophy respecting the dignity and worth of the individual. In both extremes the individual is sacrificed, on the one hand to the power of the bureaucrat, on the other to the power of the entrepreneur. Is there a middle course? If there is a middle way, it lies not with an all-powerful government employing as civil servants its teachers and its doctors, its lawyers and its engineers, and ultimately stifling these all-important areas of personal freedom. If there is a middle way, it lies not in the unrestricted power of the entrepreneur to whom the burden of the distribution of social services becomes an intolerable restriction on profit.

Alfred North Whitehead[4] wrote: "The effectiveness of a solution to this dilemma demands institutions founded upon professional qualifications. The most important function of professional institutions lies in the supervision of standards of individual professional competence and of professional practice. In this area the problem of personal freedom is resolved. For it is not opinions that are censored but the degree of learning and ability. Thus, in the more important fields of thought, opinion is free and so are large differences of practice. Society is thus provided with objective information as to the sort of weight to be attached to individuals and as to the sort of freedom of action that may safely be granted. Whatever is done can be subjected to the test of general professional opinion acting through its institutions. The impact of this professional freedom can be important to non-professional areas. For the professional organizations should be able to demonstrate the dangers of extravagant notions."

It was a professional organization, the Canadian Bar Association, in assembly that felt free to censure the Canadian Government's handling of the post-war spy trials, by the following resolution: "It is

recommended that the Association go on record in uncompromising support of the rule of Law, and of strongly disapproving any action by government or by any individual or organization which infringes in any degree the freedom of the subject under the law."[5]

As an example, in the teaching profession neither the general community nor the government is competent to determine either the subject matter to be taught or the permissible deviations to be allowed. Nor can the community or the government determine individual competence. There can be only one appeal. This is to the general professional opinion as indicated by the practice of accredited professional institutions. The State of Tennessee did not err in upholding the principle that there are limits to the freedom of teaching in schools and colleges. But it exhibited gross ignorance of its proper function when it defied a professional opinion which was practically unanimous.

Professional organizations thus became a bulwark against the invasion of individual freedom. In a world of growing restrictions there is need of such bulwarks, a need far greater than the average man realizes.

Excellence—a Common Meeting Ground

Professional organizations, because they are born out of universities, whose central creed is aptly summed up in a single phrase "the striving for excellence", can be a unifying influence in a clashing, strident world of opposing political ideologies. Excellence is the common meeting ground, the common denominator of all professional organizations, be they East or West.

There is much less separating physicians, teachers, lawyers and engineers true to their professional credo, from whatever corner of the world they derive, than there is between their respective politicians made rigid by fixed attitudes. Witness the cultural and scientific exchange that can go on, even if limited by security considerations, in a bi-polar world. This is an avenue that can never be closed, that may yet lead to the broad highways of peace. And there is hope that this may be an avenue to some common ground between clashing ideologies not in outer space, not on the moon, but right here on earth.

Summary

The development of professional responsibility had its birth in the university, was granted corporate form by the law of the land, and was given the breath of life by the aspiration toward excellence. A strong professional organization may become an important influence in the protection of freedom of the individual both within and without the profession. A profession can provide a durable bridge between conflicting ideologies.

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CASE REPORT

LIPOMATOSIS OF THE ILEOCECAL VALVE

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Lipomatosis of the ileocecal valve can be defined as the submucosal infiltration or accumulation of fat in the ileocecal region, usually resulting in non-specific gastrointestinal symptoms.

Synonyms are: Submucous lipoma of the ileocecal valve; ileocecal valve syndrome; pouting ileum; submucosal fatty accumulation of ileocecal valve; fatty degeneration of the ileocecal valve.

Etiology.—The etiology of this condition is unknown. Some writers have related it to an inflammatory process of the ileocecal region;[2, 9] others simply state that the condition occurs in obese individuals or in individuals with disturbances of lipid metabolism.[5, 6]

Incidence.—This condition occurs more frequently in women than men.[1-3] In the series of 18 patients studied by Lasser and Rigler,[2] only six were men. Lipomatosis of the ileocecal valve occurs chiefly in individuals over 45 years of age, although four patients have been reported between the ages of 30 and 43 years.[1-3] To 1959, all cases reported have apparently been in members of the Caucasian race.

Clinical features.—The condition may be asymptomatic, or the symptoms may be so insignificant that they are overlooked. The case presented in this report is an example of this condition with no apparent symptoms.

On the other hand, non-specific but definite symptoms may be present. In the cases reported in the literature, most of the patients have had long-standing gastrointestinal symptoms.[3] In Lasser and

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Rigler's series,[2] half of the patients had symptoms of chronic gallbladder disease. Colicky pain is the most frequent symptom.[2, 4, 6] The localization of the pain is apparently not reliable, however, only seven of 16 patients having pain localized in the right lower quadrant.[2] Recurrent flatulence is a very frequent symptom, as is chronic constipation; and some patients have diarrhea.[3] Severe abdominal distension, nausea and vomiting may occur as evidence of partial mechanical obstruction of the valve lumen by the lesion. Complete intestinal obstruction usually occurs only after intussusception which is then manifested by rectal bleeding; and other symptoms of complete intestinal obstruction will be present, as well as severe localized tenderness in the right lower quadrant, with or without a palpable mass. It is important to note that intestinal hemorrhage may occasionally be present without any symptoms of intestinal obstruction and may be due only to lipomatosis of the ileocecal valve.[3, 4]

A palpable mass in the right lower quadrant is not a frequent finding unless intussusception is present. During an exploratory laparotomy, the surgeon can easily overlook an ileocecal valve that is only moderately enlarged.[3, 7] However, on palpation through the cecal wall, when the lesion is suspected, the ileocecal valve has a "characteristically soft, lobulated feeling".[3]

Radiological findings.—A barium enema usually reveals a radiolucent tumour projecting into the cecum. Lasser and Rigler,[2] in their series of radiologically positive cases, included cases varying from those with only slightly enlarged ileocecal valves to those with huge filling defects in the cecum. Different radiologists have described the radiographic appearance of the valve in the following ways: an "open umbrella", a "rosette *en face*", and resembling the Greek letter epsilon.[9] It is important to note that even with a radiological appearance typical of lipomatosis of the ileocecal valve, one must still consider the possibility of some other type of tumour.[1-3, 6]

Pathological findings.—Grossly, the region of the ileocecal valve is enlarged and the mesentery is infiltrated with a large amount of fat. Within the cecum, protruding from the ileum, there can be seen a huge, pale orange or yellow mass, with the shape of a mushroom, and a small central lumen. Edwards and Zangara[6] described this lesion as resembling a "boggy cervix protruding into the vagina". Very often, there is also fatty infiltration into the adjacent wall of the ileum and/or the cecum. When there has been bleeding per rectum, there are frequently superficial erosions of the valvular mucosa.[3]

Microscopically, the characteristic finding is adipose tissue infiltrating the submucosal area between the mucosa and the muscularis mucosae or between the muscularis mucosae and the circular muscle of the ileocecal valve. The complete lack of encapsulation suggests that this lesion is a fatty infiltration rather than a neoplasm.[1] Often, there is a chronic inflammatory process in the region of the lesion.[1, 2, 8]

Treatment.—Most of the cases described in the literature have had surgical intervention, the usual procedure being a right hemicolectomy with an end-to-end enterocolostomy.[1, 3] Simple excision of the ileocecal valve has been performed with very good results.[1, 4]

An asymptomatic or minimally symptomatic lesion demonstrated radiologically should be followed closely, and if symptoms appear operation should be considered.[2, 8] One should always bear in mind that lipomatosis of the ileocecal valve may be a cause of unexplained gastrointestinal bleeding; and because this lesion is usually difficult to define by simple palpation and may be otherwise asymptomatic, careful radiological examination of the ileocecal area may provide the diagnosis.

Prognosis.—The prognosis usually is excellent. It is worthy of note that an occasional patient may have or may develop lipomatosis in another region of the gastrointestinal tract later.

CASE REPORT

R.M., a 75-year-old obese white man, was admitted to the Maryland General Hospital because of confusion and disorientation, after the ingestion of 57 grains of amobarbital sodium (Sodium Amytal) in the previous 48 hours. He had been a chronic alcoholic for about 35 years. On admission, his blood pressure was 220/128 mm. Hg, his pulse rate was 68 per minute and regular and his respiratory rate was 20 per minute. He was irritable and agitated. The pupils reacted slowly to light. The chest was barrel-shaped and there was bilateral gynecomastia. Breath sounds were decreased. The abdominal examination was negative.

Laboratory work revealed a hemoglobin of 14.5 g. % and a leukocyte count of 6050 per c.mm. with 3% stab cells and 80% polymorphonuclear leukocytes; there was slight elevation of his blood urea nitrogen, bilirubin, and thymol turbidity; a slightly decreased serum cholesterol; a negative cephalin flocculation test; and a normal total protein and albumin/globulin ratio. Urinalysis revealed 3-plus albumin, numerous erythrocytes and 25-30 leukocytes per high-power field. A serological test for syphilis was negative. The spinal fluid sugar was 73 mg. % and the total protein was 57 mg. %.

Despite supportive therapy, he developed pneumonia and a lower urinary tract infection and died on the 25th day in hospital.

External examination.—The body was that of an obese white man, weighing about 240 lb. and measuring 69½ inches in length. Pertinent findings were limited to the alimentary tract. The esophagus, stomach, duodenum, jejunum and proximal ileum were not remarkable, with no evidence of fatty infiltration. At the ileocecal junction was a mushroom-shaped, yellow, circumferential, lobulated mass which projected into the cecum for a distance of about 2 cm. and was obviously fatty on cut section. The valve orifice itself was stenotic and a finger could be inserted through

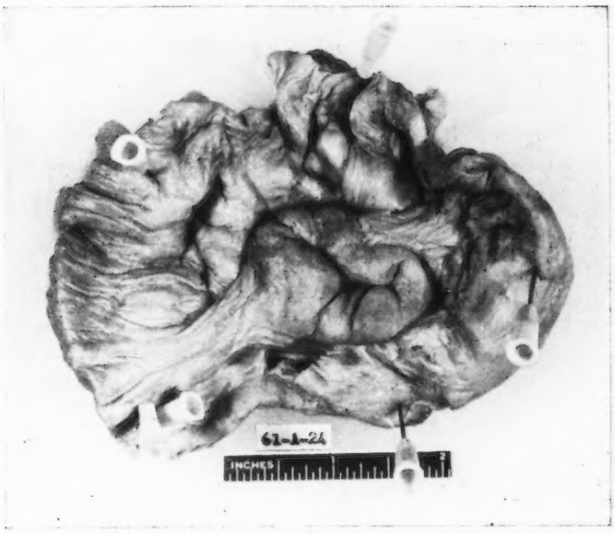

Fig. 1.—Ileocecal valve viewed from the cecum.

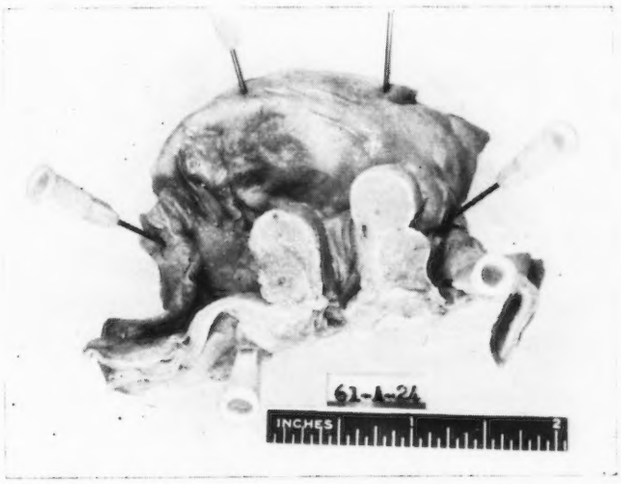

Fig. 2.—Cross-section of ileocecal valve, showing resemblance to the Greek letter epsilon (ε).

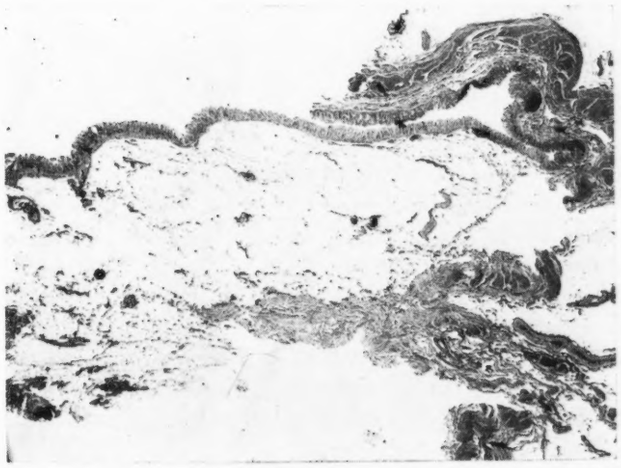

Fig. 3.—Low-power photomicrograph showing extensive fatty infiltration of the submucosa with invasion of the circular muscle layer.

it only with difficulty. There was no dilatation of the small bowel. The appendix was not remarkable. The colon showed marked dilatation, chiefly in the transverse portion, with thinning of the wall, but was not otherwise remarkable. The appendices epiploicae were prominent, and the mesentery contained a large amount of evenly distributed fat.

Microscopic examination.—A section of the ileocecal valve showed adipose tissue diffusely infiltrating the submucosal area, separating the muscularis mucosae from the circular muscle layer but extensively infiltrating both. The mucosa showed the usual number of chronic inflammatory cells but was not otherwise remarkable. The longitudinal muscle layer and the epithelium and serosa were not remarkable.

Final pathological diagnosis.—The final pathological diagnosis was as follows: cerebral arteriosclerosis with generalized cerebral cortical atrophy; bronchopneumonia, focal, right lung; pulmonary emphysema, moderately severe, vesicular, bilateral; pulmonary congestion, edema, and focal hemorrhage; lower urinary tract obstruction due to benign prostatic hyperplasia and hypertrophy, with cystitis; arteriosclerotic heart disease with coronary arteriosclerosis, moderate, and interstitial myocardial fibrosis, diffuse; hypertensive cardiovascular disease with cardiac hypertrophy, left ventricular type; portal cirrhosis, Laennec type; adrenal cortical lipid depletion, severe; nephrosclerosis, severe, benign; exogenous obesity, severe; lipomatosis of ileocecal valve.

COMMENT

A review of the available literature from 1950-1959 indicates that lipomatosis of the ileocecal valve is an occasional cause of gastrointestinal symptoms. It symptomatology is neither constant nor reliable. In cases with unexplained gastrointestinal hemorrhage, recurrent incomplete intestinal obstruction, or vague, ill-defined abdominal symptoms, the possibility of lipomatosis of the ileocecal valve should be considered. The barium enema is one of the best methods of making the diagnosis of this lesion. When performing an operation with this diagnosis in mind, one should remember that the ileocecal region may appear normal by palpation, and only a cecotomy can rule out lipomatosis with certainty.

There are three types of lipomatosis of the ileocecal valve which can be distinguished clinically: (1) those which are completely asymptomatic; (2) those with low-grade, long-standing gastrointestinal symptoms; (3) those with severe gastrointestinal symptoms due to acute or recurrent intestinal obstruction.

Cases with moderately severe symptoms and the complications such as intestinal obstruction require surgical treatment. The three possible surgical procedures which can be considered are: (1) local excision (circumcision) of the lipomatous ileocecal valve;[1, 3, 4] (2) bypass of the lesion, with a side-to-side ileo-colostomy;[9] (3) extensive resection of the terminal ileum, a right hemicolectomy, and an end-to-end ileo-colostomy.[1, 3, 4, 6]

Those cases with only mild symptoms may be treated medically.[9]

SUMMARY

A case of lipomatosis of the ileocecal valve is presented. This lesion is a submucosal infiltration of adipose tissue in the ileocecal region which may be

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asymptomatic or produce various gastrointestinal symptoms, including intestinal obstruction. The etiology is unknown. The disease occurs predominantly in women and affects chiefly individuals in the middle or older age groups. The diagnosis is best made by radiological methods, although clinical symptoms may be helpful. Asymptomatic cases are discovered incidentally, radiographically, during operations, or at autopsy. Palpation of the ileocecal valve region during exploratory laparotomy is not reliable in ruling out lipomatosis; this requires a cecotomy. In patients with unexplained gastrointestinal bleeding, lipomatosis of the ileocecal valve should be considered as a possible cause.

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SHORT COMMUNICATION

FACILITATION OF VAGINAL HYSTERECTOMY BY UTERINE BISECTION

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AFTER THE DECISION has been made to do a hysterectomy, the surgeon must choose between the abdominal and vaginal route of approach to the operation. Almost always the abdominal route is chosen for endometriosis, chronic pelvic inflammation, adnexal pathology and supra-vaginal malignancy. In other conditions, however, whether it be uterine disease or prolapse, vaginal hysterectomy should be considered.

Vaginal hysterectomy has many advantages over abdominal hysterectomy in properly selected cases: (1) repair of vaginal wall prolapse can be done at the same time; (2) obesity is not a factor in technical exposure, as there is no fat in the tissues encountered during operation; (3) there is less disturbance of the body as a whole during the postoperative period; (4) abdominal incision is eliminated; (5) any adhesions that form, postoperatively, do so in a very small area at the most dependent part of the peritoneal cavity.

After selecting the situation in which vaginal hysterectomy is desirable, the surgeon may be deterred by the possibility that "the uterus cannot be removed per vaginam". On a number of occasions the author has been called into the operating room in consultation when the surgeon has encountered difficulties while doing a vaginal hysterectomy. Having progressed past the point of no return, the operator finds that the uterus will not come down further (see Figs. 1 and 2), and naturally he is loathe to put the patient's legs down and approach the hysterectomy abdominally.

In such cases, after having divided the cardinal and utero-sacral ligaments and the uterine vessels,

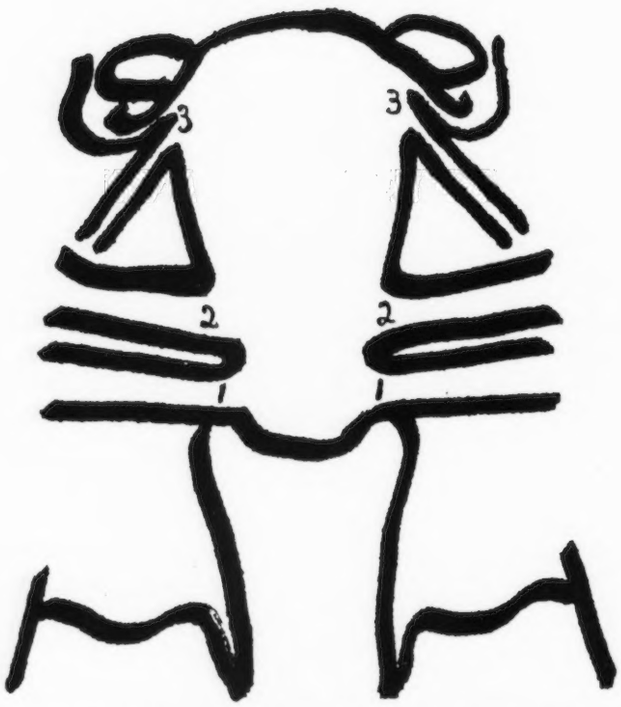

Fig. 1.—Diagrammatic representation of pelvic anatomy showing three major "pedicles" on each side: (1) cardinal and uterosacral ligaments; (2) tissue containing uterine blood vessels; and (3) broad ligament containing ovarian blood vessels, fallopian tube and round and ovarian ligaments.

there is one simple procedure which is very useful and often indispensable, namely, *median bisection of the uterus from cervix to fundus* (see Figs. 3 and 4). For the protection of bladder and rectum, a Jackson retractor is inserted into the peritoneal cavity beneath the bladder and a Sim's speculum is inserted into the peritoneal cavity in front of the rectum. A tenaculum is placed on each side of cervix and, while firm continuous traction is exerted downwards, backwards and laterally, the uterus is incised in the midline, starting at the cervix. As the incision approaches the fundus, the uterus pulls downwards through the pelvis, and the broad ligament pedicles become gradually more accessible. When the uterus is completely divided,

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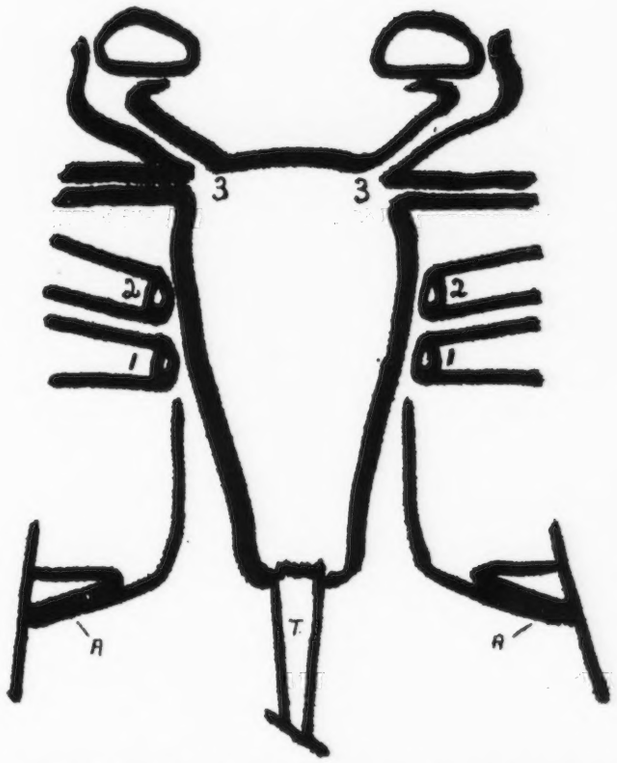

Fig. 2.—Broad ligament pedicle inaccessible. Labia minora sutures (A-A) to thighs and pedicles 1 and 2 divided. With traction on tenaculum (T.) on cervix, uterus descends through pelvis.

one half is displaced upwards (see Fig. 4) allowing sufficient space to pull the other half across the midline as well as downwards, so that the broad ligament pedicle becomes readily accessible for clamping. It is then an easy matter to draw the remaining half across the midline for clamping of its uppermost pedicle, and the hysterectomy is completed.

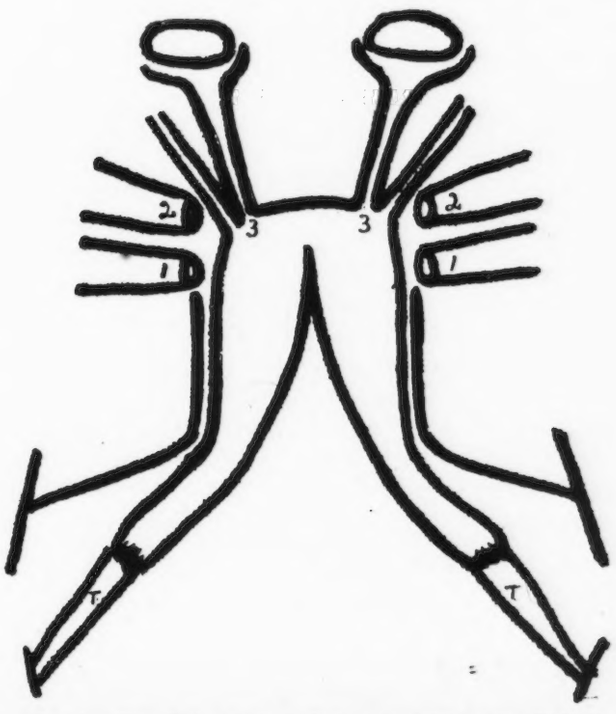

Fig. 3.—Broad ligament pedicle accessible with difficulty with Tenacula (T.-T.) on each side of cervix; uterine bisection facilitates descent through the pelvis.

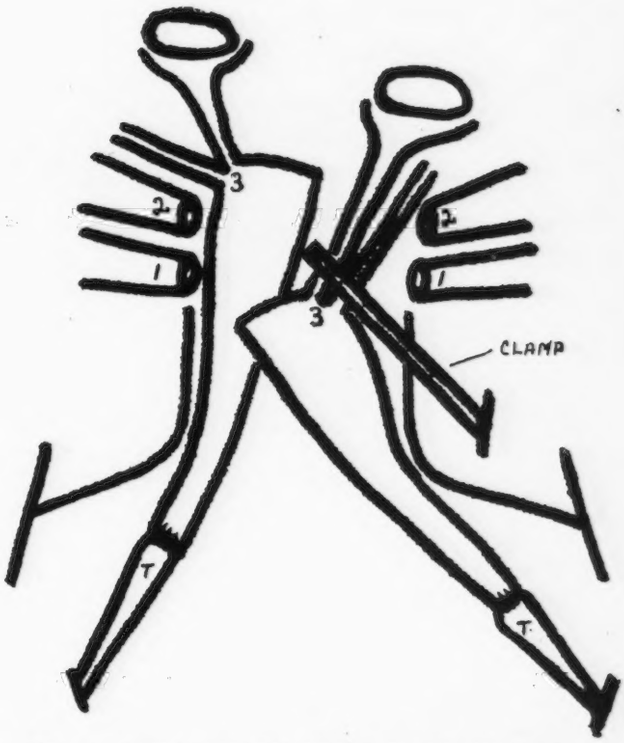

Fig. 4.—Broad ligament pedicle readily accessible. Bisection completed, right half of uterus retracts upwards while left half pulls across midline allowing space to clamp pedicle.

Often during bisection of the uterus, it is useful to enucleate a number of fibroids, thus reducing the size of the uterus and facilitating its descent through the pelvis. By this means, a uterus considerably enlarged with fibroids can be removed vaginally.

It is important in any pelvic surgery that the bladder and rectum should be empty. To facilitate exposure at the outset it is helpful to suture the labia minora to the skin of the thighs, and the fourchette to the sterile sheet in the midline posteriorly. Also in cases where the perineal body is long and firm, exposure can be increased considerably by means of a midline episiotomy. Special types of self-retaining retractors are unnecessary in performing vaginal hysterectomy. Indeed such mechanical devices often interfere with the normal pliability and "give" of the soft tissues. Pedicle clamps should be used only one at a time, ligating each pedicle as one proceeds with the operation. This keeps the number of instruments in the operating field at a minimum at all times.

Taking advantage of these techniques, particularly the procedure of bisecting the uterus, it should be possible to do a large number of hysterectomies by the vaginal route. There are centres which advocate a high percentage of vaginal hysterectomies, and others which feel that the procedure is seldom indicated. However, from a practical point of view, it is probably true to say that about half of all hysterectomies should and could be done vaginally.

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BRITAIN'S N.H.S. IN RETROSPECT

HEALTH insurance is a subject of more than topical interest to most Canadians. The recent appointment of the Royal Commission on Health Care, and the continuing work of the Advisory Planning Committee on Medical Care in Saskatchewan, indicate a searching appraisal of the need for medical services insurance and the methods which Canadians and others have used to meet this need.

It was, therefore, with great interest that we read "The Genesis of the British National Health Service",[1] the first of a promised series of essays on health services by John and Sylvia Jewkes. Mr. Jewkes is the Professor of Economic Organization at Oxford University, and was a prominent member of Britain's Royal Commission on the Remuneration of Doctors and Dentists which reported in 1960. Mrs. Jewkes is a charming and knowledgeable co-worker in this field of medical economics, to the study of which both have contributed much time and effort during recent years.

The "Genesis" of the Greek translators has likely caused less conflict of opinion than will arise from the frank comments and critical analyses which these authors have portrayed. Two editorials in leading British medical journals have taken opposite views of this publication. The editor of the *British Medical Journal* in large measure agrees with the provocative statements which are made;[2] *The Lancet* is very critical of the inferences drawn.[3]

The Jewkes undertook a difficult task. Such self-examination is not likely to become widely practised. Each of us tends to have, whether we admit it or not, a convenient memory.

Proponents of the National Health Service point to the achievements of the period of its existence, ascribe them to the operation of the Service, and conveniently forget its defects. Critics, too, belabour their concerns, but as the essay reveals, they display a curious ambivalence in their acceptance of the system, while expressing their dislike of its results.

The essay comments on three phases of N.H.S.—the rationale of the profession, the sociologists and the politicians in proposing its introduction; the progress made in achieving its objectives; and a comparison with conditions in the United States, with some indulgence in speculation on "what might have been".

Each of these phases can provide lessons for Canadians. Britons before the Second World War, like some Canadians today, considered that the medical system was seriously defective and that nothing short of a centrally controlled, tax-supported system could provide the appropriate remedies. Interestingly, the profession, or at least a substantial part of the profession, agreed with this thesis, and a draft report of a commission, set up by the British Medical Association and the Royal Colleges, envisaged, in 1943, a central authority concerned with all medical services and a chain of health centres with salaried doctors.

The Jewkes's examination of these circumstances indicates that the medical services existing before the war were not as inadequate as many believed and compared favourably with those of the United States in many respects. The poor were well cared for, and the burden of any neglect fell on the middle class.

Our only criticism of this analysis of N.H.S. is that it does understate certain improvements realized by the service. It is impossible to survey the operation of the service without being aware of substantial achievements in the provision of consultants' services. The Jewkes's critique is, however, more subtle. It is not concerned with apparent manifestations of progress but rather tries to relate these to the reasons postulated for the introduction of the service. In this connection it notes that the greatest increase in the utilization of services has occurred among very old men and among women up to 35 years of age. This suggests to the Jewkes that there was not widespread medical neglect before the introduction of the National Health Service, and that such gaps as did exist were probably to be found among the dependents of wage-earners who were not covered by the pre-existing National Health Insurance Scheme.

Professor and Mrs. Jewkes make some interesting comparisons between the United States and Britain on a "before and after" basis. They comment that before the war, Britain led the U.S.A. in the provision of hospital beds. Today this situation is reversed. They indicate that before the war the U.S.A. spent a larger percentage of its national income on health services than did Britain, and that the disparity between the two has increased, as the U.S.A. has continued to increase the proportion of its national income devoted to these services, whereas Britain has not.

This points up one of the basic problems of state-financed medical care programs. As a result of the

constant competition between varied state responsibilities for the available moneys, the amount allocated to a medical care program may not be sufficient to meet the needs of the service. The Jewkes state this concern in other words, indicating certain reasons for suggesting that the National Health Service has positively hindered the growth of medical services in Britain.

Professor Jewkes may be classified as one of the dissident economists who look coldly and critically at N.H.S. and who ask themselves whether the nation is obtaining full value for the money and effort expended in making it work. His views are worthy of close attention in the current Canadian context, and we shall look forward to further monographs from the family pen. B.E.F.

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LUNG CANCER: 1881 TO 1960

IT IS generally accepted that the increasing number of recorded cases of pulmonary carcinoma is a result not only of improved diagnostic accuracy, but that it reflects as well a real increase in the incidence of this disease. It is also a commonly held concept that lung cancer can be classified with relative accuracy into distinct histological types which differ fundamentally in their etiology and behaviour. The recently published results of a critical, long, hard second look at these two prevalent assumptions are worthy of note.[1]

From a review of pathological records in the *Transactions of the Pathological Society of London*, for the years 1881 to 1900, it was apparent that in the later decades of the last century bronchial carcinoma was not a rare disease, although it was rarely identified as such. In the records for the year 1888, for example, a confident retrospective diagnosis of bronchial carcinoma could be made in seven cases, although only one of these was diagnosed as such at the time.

In the period from 1901 to 1930 pathologists became increasingly aware of the real prevalence of bronchial cancer, of its diverse and misleading clinical manifestations and of its variable and often "sarcoma-like" histological appearance; the common "oat-cell" tumours were recognized for the first time as carcinomas and not sarcomas. It was postulated by the author of this study that the fourfold increase in the number of lung cancer death certificates which took place during these decades could be attributed in large part to this increased knowledge of the pathological vagaries of this disease.

In the last three decades, from 1931 to 1960, many further advances have been accomplished, not only in the field of pathology, but also in the expertness of clinical diagnosis. Special chest clinics and thoracic surgery units have been established with highly developed diagnostic facilities and techniques in radiology, bronchoscopy, and cytological and biopsy methods at their disposal. However, the most important advance during this period is related to the increase in "lung cancer consciousness" on the part of clinicians as well as pathologists. Yet even today, with all of these facilities and with an increased knowledge and awareness of the disease, lung cancer still evades clinical diagnosis in a considerable number of cases that ranges from 26 to 42% in several reported series.

Undoubtedly a large proportion of the increase in registered deaths due to lung cancer which has occurred since 1900 is due to more accurate diagnosis and greater clinical awareness of the disease, but it is impossible to assess retrospectively just what proportion of clinical and pathological misdiagnoses were made at any given time, and even now this proportion is still substantial. Therefore it is not, and possibly never will be, known whether improved diagnostic acumen accounts for the whole of this increase. Results of British and American studies on the comparative risks of lung cancer in smokers and non-smokers provide impressive evidence that smoking is an important etiological factor in modern-day pulmonary carcinoma and that this conclusion would be valid whatever the trend of the incidence of the disease, even if this trend were declining.

The questionable validity of arbitrary histological subdivision of various types of lung cancer is suggested by the great diversity of such classifications that have been adopted by different pathologists, and especially by the widely differing percentages of tumours allotted to particular subgroups by different observers. A review of the histological structure of pulmonary carcinoma confirms that in its histological structure lung cancer is highly pleomorphic, and that its subdivision into histological types is often based on highly arbitrary criteria. In various series, heterogeneous structure has been observed in from 23 to 52% of these tumours. Further, while some claim that a rough correlation can be demonstrated between the histological structure of the tumour and its site, sex incidence and metastatic behaviour, exceptions to any such attempted correlations are all too common. It would be premature at the present time to attempt to draw any firm conclusions regarding the correlation of the etiology of the tumour and its histologic type before more intensive study and critical appraisal of the structural versatility of pulmonary carcinoma have been carried out. F.L.

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WESTERN MEDICINE IN THE TROPICS

ONE of the principal ways in which Western civilization has made an impact on the East has been through the provision of medical care. But, despite an extending network of medical facilities and the greater efficiency of modern drugs, scientific medicine is not making progress everywhere. In China, for example, Western medicine is in retreat before the traditional medicine promoted by the Government. One explanation for the official promotion of traditional medicine in China is that it is less expensive; the traditional remedies are infinitely cheaper and as placebos are more effective because they are rooted in local beliefs and customs.

Some of the reasons for the shortcomings of Western medicine when it attempts to serve a tropical people are examined by Klokke (*Lancet*, 1: 1336, 1961), who believes that expense, dislocation of the family pattern by centralized treatment and the impersonal nature of scientific medicine are all contributing factors.

The particular difficulties facing preventive medicine are related to the inability of the health workers to involve the people in the programs designed to eradicate disease. Governments and international organizations try to counteract the vast amount of illness present on every hand by conducting mass campaigns against endemic diseases. Where environmental sanitation is virtually absent, lasting success in such campaigns often depends on individual health behaviour; and for this reason "health education" becomes an important function of the medical services. But the result in actual fact is that *demands are made upon people in the tropics which cannot be satisfied even in a Western environment.* For instance, in America, the sociologist Lomon Koos (1954), in a survey of health attitudes in the State of New York, reported that a public-health worker said: "I wish everyone in Regionville felt as interested in health as we professional people do. Sometimes it is like butting your head against a stone wall trying to get something through the heads of even the 'best' people."

In Western surroundings deficient health behaviour matters less because of the environmental sanitation which produces safe drinking-water, and removes feces and refuse efficiently. Moreover, the list of such external "advantages" is always growing. For example, a professor of pediatrics, commenting on the high bacterial count found in bottle-feedings prepared by the mother, recommended that these feedings should be prepared by industry. This advice assumes that it is easier or better to bring about necessary changes by altering the external environment for all, even when only a minority are at risk. *Apparently in the West no one concentrates any longer on achieving alterations in individual behaviour.*

That the danger of making excessive demands upon a tropical society is not imaginary is illustrated by a remark of such an authority as Cicely Williams (*Lancet*, 2: 919, 1958). One of her objections to mass campaigns is that these do not encourage people to "associate improvements with their own responsibilities or with alterations in personal and community behaviour". And no doubt she is right in saying that at the end of such a campaign health behaviour is often no better than it was at the beginning. But can we fairly blame the campaign for not being able to modify people's habits?

Even in the Regionville of Lomon Koos—which is healthier than a tropical area after a mass campaign—the necessity for modified health behaviour (and the difficulty of bringing it about) is very clear. There, health behaviour is related to social class, and the attitude of labourers (class III) closely resembles what is often seen in the tropics:

"In Regionville, class-III people are reluctant to call in medical help. They were asked what they would do in the face of certain symptoms of disease. For more than half the number of symptoms enumerated, only a quarter of the families declared they would probably call in medical help. Calling in help was influenced by factors like fear (of operation or of going to a hospital), and the uncertainty about the expense. The position in the family was important, help being more likely to be called for the husband 'who earns the money' than for the housewife. Personal experience with a particular symptom made people familiar with the complaint and prevented their calling in help. Group experience also guided people's inclination to be treated. The reason why three-quarters of the families of class III would prefer the 'chiropractor' was determined by the psychological relation between healer and patient."

The difficulties facing the health worker in the tropics are also present in the West, despite our many material advantages. The twin concepts, good health as the sixth freedom and the highest quality of medical care as the inalienable right of every citizen, are being accepted by our society as reasonable political goals. These concepts cannot be realized solely through the increased application of external remedies such as environmental sanitation, mass immunization, and intensive therapeusis, effective though these measures have been in the past. If the architects of the new era of total good health rely on these externals only, they will be pursuing a ruinously expensive mirage. The aims of health maintenance and prevention of degenerative and other diseases requires the continuous, informed co-operation of every citizen in a lifelong program; this envisions "public health" on a scale undreamed of in the past. Preliminary research into the methods of public health education has had scant support in the past, and our greatest weakness is our inability to persuade the public that good health has, as part of its cost, continuous individual effort.

Letters to the Journal

AUTOPSY ON A MURDER TRIAL

To the Editor:

This letter is with reference to "Autopsy on a Murder Trial" in the Editorials and Comments section of the July 22 issue of the Journal (*Canad. M. A. J.*, 85: 205, 1961)—a commentary on "Ten Rillington Place" by Ludovic Kennedy.

It is not difficult to agree with the commentator that "Ten Rillington Place" is "good reading for any medical man who enjoys a well-flavoured London detective story." In the same building, on the top floor, Evans's murder of his wife and child; on the ground floor, Christie's murder of his wife and five other women; a body buried under the floor in the living-room; three bodies hidden in a sealed cupboard in the kitchen; two bodies buried in the yard; carbon monoxide poisoning; and stories of abortion and of suicide by poisoning, should satisfy the most difficult to please reader of such stories. But that the book is "perfectly true" and "obligatory reading for coroners, forensic pathologists and psychiatrists" hardly accords with the facts.

Of these two trials, I have, verbatim, all of the evidence, the closing addresses to the Juries by the Prosecution and the Defence and the Judges' Charges to the Juries; verbatim, the Judgment of the Criminal Court of Appeal in the case of Evans; the Reports of the special investigation for the Secretary of State for the Home Department, and the Debates in the House of Commons on whether or not there had been a miscarriage of justice in the execution of Evans; a variety of other matters, including developments after the trial and conviction of Christie, such as his statements to the Anglican Prison Chaplain which, having not been made in confidence, were reported, with the approval of his Bishop, to the authorities.

"Wholly convinced of Evans's innocence," the author commences "Ten Rillington Place" with an "Open letter to the Home Secretary" in which he reflects upon the integrity of the Lord Chancellor, Lord Kilmuir, who at the time was Secretary of State for the Home Department. And, as examples of the emotional character of the book, "highly prejudiced", "a monstrous thing to say", "It is appalling that any English judge should have so greatly distorted the truth" are of the milder of the things the author says of Mr. Justice Lewis before whom Evans was tried.

In "Autopsy on a Murder Trial", Evans is referred to as a "lad". In "Ten Rillington Place", he is "a tiny little fellow" and a "high-grade mental defective". For some reason, it seems conventional to refer to anybody accused of a capital crime as "this girl" or "this lad", provided she or he is still under 60 years of age. Over age 25, married, father of a 14-month-old child, and his wife in her fourth month of pregnancy with another, hardly fit in with boy, youth, stripling, which the word "lad" generally means. Also, height 5′ 5½″ and weight 140 lb., is not quite the pattern of "a tiny little fellow". Nor does a "high-grade mental defective" accord with the facts. When one studies carefully Evans's different confessions and his skilful evasions in the cross-examination by counsel for the Crown, here is seen no high-grade mental defective, but a person very alert to the implications of many of the questions which he had been asked. "A very lively imagination . . . with very little regard for the truth" is the way the Judge put it in his Charge to the Jury. Nor was "a high-grade mental defective" the conclusion arrived at by the Board whose duty it was, after Evans had been sentenced to be hanged, to determine Evans's mental state, and thus whether they could recommend reprieve. For this purpose, they had, in addition to interviews with Evans, all the records of the case and also all of those of his conduct in prison. And with all of this information before them, all three psychiatrists had come to the conclusion that Evans was not a mental defective. He was uneducated—he could neither read nor write (except sign his name); he had a history of poor health; but he was quite well-informed about things of common interest.

For reasons to be noted later, Christie had testified at his own trial that, like some of his other victims, he had rendered Evans's wife unconscious by gassing before he had strangled her. Absolutely certain, therefore, for this and for other reasons, that an innocent person had been hanged, the author of the book overlooked the inconsistency between this belief and the postmortem findings. Carbon monoxide disappears very slowly after death, and thus may be detected at long intervals by chemical and spectroscopic examination—three to four months is the usual time, and cases of six months and still longer are on record. Yet, despite the fact that Evans's wife's body was examined 24 days only after her death and that no carbon monoxide was found, according to the author "it seems almost certain" that Evans's wife had been gassed before she was strangled.

In the realm of imagination, and here also inconsistent with the postmortem findings, is the reference to blood which Evans had testified he had seen on his wife's body. Evans had testified that Christie had attempted an abortion upon Mrs. Evans, and that he had seen blood "on the top of her legs"; also, there was bleeding from her mouth and nose. The autopsy, however, showed "no interference whatsoever" with the pregnancy. Therefore, to account for the blood "on the top of her legs", the author says this: "It is not impossible that Christie . . . smeared blood from the face on to the bottom part to give greater verisimilitude." The fact that Dr. R. D. Teare, who had performed the autopsy, had found no blood at all—"it [the alleged abortion] left no mark which I would expect to find"—appears to the author to be of no significance.

Necrophilous intercourse is not suggested as a possibility, but is given as a positive fact. Christie, says the author, was "a necrophilic strangler". In "Autopsy on a Murder Trial", the skull and femur which had been found in Christie's yard "were relics of earlier essays in . . . necrophily". And in the cases of the murders between December 14, 1952, and March 6, 1953, it is positively asserted that Christie had "had necrophilous intercourse just after death". But what are the facts?

The most that Dr. F. E. Camps, who had performed the autopsies, was prepared to say about the woman MacLennan was that sexual intercourse had occurred

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either shortly before or after her death. In the case of the victim, Maloney, Dr. Camps's opinion was the same. In the case of the woman Nelson, there is nothing in Dr. Camps's evidence about sexual intercourse before or during or after strangling. To note also is that all of these three women were prostitutes. The spermatozoa, therefore, which were found in them at the autopsies were, *per se,* not proof that Christie had had intercourse with them. They may have been Christie's; but they may have been from someone else; or they may have been from a number of men. Also, difficult to understand, in the case of Maloney and Nelson, was the finding by Dr. Camps, between the legs of each, clother-material "in the position of a diaper".

In "Autopsy of a Murder Trial", there is the observation: "there was some evidence that Mrs. Evans had been a victim of one of Christie's necrophilous assaults. Although Dr. Teare, the very experienced police pathologist, reported his findings, they were never followed up. Indeed they were ignored by prosecution and defence alike." The question which may well be asked here, therefore, is: What grounds were there *not* to ignore them? What is peculiar about evidence of intercourse in a woman who, up to the time of her death, had been living with her husband?

The only evidence that Christie had had intercourse with his victims was Christie's own testimony, and, where it is not vague, it points not to intercourse after the murder, but murder during the intercourse—sexual frenzy of sadism. In the case of the woman Fuerst, the evidence was: "I got on to the bed and had intercourse with her. *While* I was having intercourse with her, I strangled her . . ." About the woman Eady, the evidence was: "I believe I had intercourse with her *at the time* I strangled her." Of the other three women, in the case of Maloney, it was "I don't remember really." In the case of Nelson, to the question: "Is your mind clear about what happened . . .", the reply was, "No, it is not". And in the case of MacLennan, to the question, "Do you remember anything about sexual intercourse?", the reply was "Well, I have got a vague recollection, but I cannot honestly say I did."

In his effort, in accordance with his duty, to do all possible for his client, counsel for the Defence put the suggestion of necrophily to the two psychiatrists for the Crown, Dr. J. C. M. Matheson and Dr. D. Curran; but it did not meet with success. Immediately following the question put to Dr. Matheson, the Judge asked a question which made it clear to the jury that he was differentiating between intercourse followed by strangling and strangling followed by intercourse. Dr. Curran's reply emphasized this more specifically. In his opinion, Christie's object was not to kill and then have intercourse, but, by the gassing, merely to render his victims "unconscious . . . possibly because he did not want them to know that he was impotent."

But transcending all in significance, in my opinion, was the evidence of Dr. J. A. Hobson, the psychiatrist who had testified for the Defence. Christie's defence was insanity. Therefore, as it was in his interest to state that he may have committed more murders than it was known he had committed—"the more, the merrier", as he put it to the Prison Chaplain, after his trial—so, with insanity the defence, it was in his interest to confess to necrophilous intercourse. And it is almost inconceivable that counsel for the Defence had not discussed this with his expert witness, Dr. J. A. Hobson. That counsel had it in mind is clearly seen from the questions he had put to the medical experts for the Prosecution in cross-examination. Yet, though Dr. Hobson had examined Christie "ten or twelve times"; had heard all the evidence at the Magistrates' Court; had been present each day at the trial; had read and studied all of the depositions; had been given every assistance at Brixton Prison to see Christie whenever he considered it necessary, in the whole of the examination-in-chief, counsel for the Defence did not ask his own medical expert witness a *single* question about necrophilous intercourse.

With reference to "an old femur lying about the yard" and "the skull that was in the bottom of his trash-can"—remains of two murders committed some years before by Christie—in "Autopsy on a Murder Trial" is apparently the belief that had the police known about them at the time of Evans's trial they would have been on Christie's track long before he had killed his wife and the three other women. To note here, however, is that the murders of the women Fuerst and Eady had been committed during World War II and that, because of the heavy bombing to which London had been subjected during the war, for a number of years after the war the occasional finding of a part of a human skeleton in a backyard in London excited very little curiosity. That Christie had counted on this is suggested from the fact that, when, in digging his garden several years after these murders, he found the femur, he did not bury it again, but deliberately used part of it as a prop for a fence-post. Also, when, in 1950, he came across the skull of the woman Eady, which his dog had dug up, he did not bury it, but deliberately threw it into a house which had been bombed.

The police were not the only persons who were deceived by Christie. Dr. X., who knew Christie and had been his physician during a period of 18 years, in a letter to another physician on March 18, 1952, wrote: "I wish to point out that he is a very decent, quiet-living man, hard working and very conscientious." By March 18, 1952, Christie had murdered the two women, Fuerst and Eady, and had buried them in his garden.

Certainly two persons living in the same building and committing murder by the same method—strangulation—was a remarkable coincidence. The probability, therefore, is that, had the authorities known, at the time of the murders of Evans's wife and child, that Christie had murdered two women, Evans would not have been brought to trial, or, at least, would not have been executed, for it was very largely Christie's evidence that had convicted Evans. But this would not have meant that Evans was innocent. It would merely have been fortunate for him that this remarkable coincidence had occurred.

To this day, there are persons who believe that Evans was innocent. Only last June, the trials of Evans and Christie were again debated in Parliament, in which, in the belief that Evans was innocent, it was pleaded, on behalf of Evans's aged mother, that she be allowed to remove Evans's remains from the prison grounds and give them burial in ground consecrated by her church. The Home Secretary, the Hon. Mr. R. A. Butler, stated that, in the absence of a free pardon, he could not agree to the removal of Evans's remains from the prison grounds, and the Debate ended without a vote.

The legal aspects of these two trials are many, and I am not a lawyer. But, to a layman, when all of the

records of these two trials are studied carefully, and also other matters which had come to the attention of the authorities after Christie had been executed, the evidence seems overwhelming that, in the execution of Evans, there was no miscarriage of justice. To note is that, even assuming, for argument, that Christie murdered Evans's wife, there is still the murder of Evans's child to account for, and Evans was tried not for the murder of his wife, but for the murder of his child.

In all, therefore, though, as the commentator in "Autopsy on a Murder Trial" has it, the recently published book by Ludovic Kennedy has all the qualities of the best type of British murder story, it does not, in every respect, appear to be "perfectly true" and, therefore, for coroners, forensic pathologists and psychiatrists "obligatory reading".

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COMBINATIONS OF PHARMACEUTICALS

To the Editor:

The article by Straker and Grauer in a recent issue (*Canad. M. A. J.*, 85: 127, 1961) concerning the new antidepressant combination, tranylcypromine-trifluoperazine (Parstelin), has prompted me to join the growing outcry against the tremendous deluge of shotgun combination drugs which the pharmaceutical industry has heaped upon us.

The problem of drug overdosage, both accidental and intentional, is daily becoming a more confusing one, because of the phenomenal mushrooming growth of the drug industry in producing complex and varied products. The physician is often at a loss to know how to manage comatose patients who have ingested these new products. The cut-and-dried treatments for salicylate or barbiturate overdosages are now things of the past, with the newer drugs containing two, three or even more potent chemical ingredients.

The risk of overdosage is particularly real in the depressed patient, and it necessarily follows that antidepressants prescribed for such patients offer ready-at-hand material for the potential suicide.

In the past six months at the Toronto East General Hospital the staff has encountered at least two fatalities positively attributable to overdosage of tranylcypromine-trifluoperazine (Parstelin) which had been prescribed to the patients in private practice. Both cases presented with coma and parkinsonian symptoms on admission or shortly after.

Straker and Grauer state in their article, concerning side effects, that "Evaluation of these effects is complicated by the fact that Parstelin is a combination of two drugs, and it is sometimes difficult to know which of the two is responsible for the undesirable side effect." The difficulty is certainly compounded when a potentially lethal dose has been administered.

Each pharmaceutical company which manufactures a new drug presumably should be the most informed source concerning advice regarding specific treatment of overdosage. This information for obvious reasons is always lacking in pharmaceutical literature, and until enough physicians are faced with the problem of treating bizarre overdosages, and put sufficient pressure on the industry to provide such information, I am afraid we will continue to be plagued with glossy brochures advocating "Alice in Wonderland" products which may be gobbled up like candies by young and old alike with utter abandon.

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Deep River, Ont.

To the Editor:

Dr. Robertson's letter regarding overdosage, with special reference to the ill effects of pharmaceutical combinations, draws attention to an important clinical problem. I would certainly agree with him that as side effects and especially as fatal results of drug usage become known, this information should be immediately made available to clinicians, not only via journal reporting but as notes of special caution in the pharmaceutical brochures being distributed for promotional purposes. This is an ethical responsibility which squarely faces drug houses.

Dr. Robertson's rather derogatory comments about new drugs should be evaluated in a larger sense. The development of these new drugs has markedly changed the nature of psychiatric practice by reducing morbidity and suffering, and the need for prolonged hospitalization in many patients. Undoubtedly, these drugs are potent agents, producing undesirable effects in some, and very rarely a fatal outcome. Yet there is hardly a procedure in medicine which is universally safe. This is not an apology for disaster. On the contrary, it points up the need for continuous responsible observation, and careful and cautious supervision and evaluation by the clinician in his management of every patient.

The risk of overdosage in depressed patients as mentioned by Dr. Robertson is certainly there, but the antidote is not the elimination of potent drugs. Accurate diagnosis should be followed by measures of treatment which are judged to be effective in protecting the patient and in treating the underlying depression. An obvious preventive step is not to place suicidal agents, in the form of potent drugs in large amounts, in the hands of the patient who presents this risk. However, we must also recognize that the suicidal patient is not always so diagnosed, even after careful appraisal. Even when there is a recognizable danger, this is sometimes faced by the doctor as a calculated risk, weighed against the disadvantages and remote effects of safety-minded measures. The surgeon faces the same dilemma in making decisions about the care of his patients. This disagrees with Dr. Robertson's implied solutions to a difficult problem, but admittedly leaves the problem still up in the air.

Dr. Robertson has reported two fatalities "positively attributed to Parstelin overdosage". I regret that his letter does not include some details of these cases, as this would represent a useful report, while his general statement on this matter is not. Deaths with Parstelin had to my knowledge occurred only as the result of the combined use of imipramine (Tofranil) and Parstelin. This was reported at the recent Canadian Conference on Anxiety and Depression (in June 1961) and in a report of a case by Dr. Babiak (*Canad. M. A. J.*, 85: 377, 1961). It is worth repeating that it is dangerous to use Tofranil and Parstelin together or in close succession that allows for any overlap of drug effect.

In our paper, Dr. Grauer and I drew attention to the high incidence (nearly 50%) of side effects in our

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aged chronically ill group, and emphasized the need for a cautious use of Parstelin in such patients. I have no doubt that further experience with this drug, as with any other, will clarify the dangers in its use, as well as indicate a more specific range for patient selection. At the present time, we must accept the facts of life, which from the standpoint of our medical practice include many new and initially perplexing drugs. It makes medical practice more demanding, but certainly more challenging and rewarding than was the case when we had only quinine, aspirin and barbiturates to combat disease.

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MEDICAL NEWS IN BRIEF

ACUTE HEMORRHAGE AND NECROSIS OF THE INTESTINES ASSOCIATED WITH DIGITALIZATION

A recent paper in *Circulation* (23: 358, 1961) by Gazes *et al.* reports acute hemorrhage and necrosis of the bowel in 11 patients who had been receiving a dosage of digitalis; seven of them had definite evidence of digitalis toxicity. Digitalis was considered to be the main associated factor, especially since there was no mesenteric arterial involvement and, in four cases, there was no congestive failure at autopsy. Hepatic vein or sinusoidal sphincter constriction, with resulting portal splanchnic venous congestion, was considered as a possible mechanism by which digitalization could have produced this syndrome.

This condition should be suspected when a patient develops abdominal pain while receiving large amounts of digitalis. Unnecessary surgery may thus be avoided. Frequently a diagnosis of mesenteric thrombosis or embolism is suggested by the clinical picture, but abdominal examination and flat plates do not reveal any characteristic diagnostic feature. An antiemetic tranquillizer drug is often given during digitalization, and the early nausea of digitalis toxicity may thereby be masked, as occurred in one case. Also, maintenance doses of digitalis alone can produce toxicity in the presence of potassium loss, such as occurs with diuretic or steroid therapy.

PATHOLOGICAL AND ANATOMICAL FINDINGS OF MULTIPLE SCLEROSIS IN CASES NOT DIAGNOSED CLINICALLY

Disseminated sclerosis has been on the increase in the last few decades in Central Europe. At the Pathological Institute of the University of Basle there were in the years 1940 to 1949, 30 cases of disseminated sclerosis diagnosed among 12,867 autopsies (2.3%) as against 66 cases diagnosed in 1950 to 1959 out of 15,644 autopsies (4.02%). There has also been an increase in the number of cases of "formes frustes" of disseminated sclerosis which failed to show the typical clinical picture and which ran a course with very few symptoms.

A study was carried out by Georgi (*Schweiz. med. Wchnschr.*, 91: 605, 1961) to determine how frequently such a course occurs and how frequently disseminated sclerosis is diagnosed as an accidental finding at autopsy. Of the 66 cases diagnosed in the years 1950 to 1959, only 46 were recognized clinically. Six others were given a different neurological diagnosis, such as myelosis, brain tumour, amylotrophic lateral sclerosis or spastic paresis due to cerebrovascular insufficiency. Twelve cases were completely missed clinically, and in two the condition was found at autopsy after a traffic accident. Of these 12 cases not recognized clinically, 10 were in males and two in females. All except one were older people, the exception being a 46-year-old male. In one case there was the possibility of an early symptom at the age of 25 when an epileptic form of attack occurred. Paresthesias of the fingers occurred in one patient at the age of 43, and trigeminal neuralgia in another patient at the same age. All of the other symptoms that could possibly have been due to disseminated sclerosis occurred only after the age of 50. In none of these patients was there any evidence of involvement of the eye, and no intention tremor or speech defect was recorded. Temporal pallor of the optic disc, absence of abdominal reflexes, spasticity of extremities were not described.

ANURIA AS A PRESENTING SYMPTOM IN UNSUSPECTED LEUKEMIA

Elevated serum uric acid and increased uric acid excretion are frequently present in the myeloproliferative disorders. During treatment of leukemia with radiation, alkylating agents and certain antimetabolites, uricosuria may rise to dangerous proportions and symptoms of acute gout may occur. This is assumed to be due to an accentuation of hyperuricemia because of increased nuclear destruction. It has been stated that the incidence of uric-acid stones in patients with the myeloproliferative disorders is 75 times higher than that in the normal population. In one study of 283 patients with these disorders, renal calculi were found in 5.3%. These stones usually develop under therapy but have been seen in patients with untreated leukemia. In the study just referred to, ureteral obstruction was not present in any of these untreated cases. In the differential diagnosis of anuria, bilateral ureteral obstruction with stones is routinely considered, as in a recent case report by Post (*New England J. Med.*, 264: 1253, 1961) which described a 78-year-old man in whom anuria, as a consequence of bilateral ureteral obstruction by uric-acid calculi, was a rare presenting symptom of acute leukemia.

ANTICOAGULANT THERAPY IN CEREBROVASCULAR DISEASE

Some of the early reports on the use of anticoagulants in the management of patients with cerebrovascular disease suggested that anticoagulants produced striking benefits in reducing attacks of cerebral ischemia and in reducing the fatality rate, but others were not convinced of this. The main obstacle to the widespread use of anticoagulants in cerebrovascular disease, apart from the expense, is the fear of causing hemorrhage. Although the danger of producing hemorrhage into the infarcted heart by the administration of anticoagulants to patients with coronary disease appears not to have been investigated, it is noted that in a large series of patients with coronary disease treated with anticoagulants, one case of cerebral hemorrhage occurred. Experimental work seems to show that there is a real danger that an ischemic brain infarct might become hemorrhagic under the influence of anticoagulants. It is evident that the evaluation of the results of anticoagulant therapy must be based on careful clinical observation combined with precise diagnosis, and the slightest suspicion that the cerebral disorder is hemorrhagic constitutes an absolute contraindication to anticoagulants. In one controlled clinical trial, fatal hemorrhages occurred in five patients receiving anticoagulants, but none occurred in control cases. While these hemorrhagic fatalities could conceivably have been due to errors in the presumptive diagnosis of thrombosis, the fact that the incidence of other, non-fatal, vascular disorders was no greater in the control group than in the treated group suggests that there is no clear clinical advantage to be set against this risk of presumed misdiagnosis.

Thus, comments an editorial in the *Brit. M. J.* (1: 1094, 1961), there are still doubts about the effectiveness of long-term anticoagulant therapy in cerebrovascular disease, and in myocardial infarction as well. Such doubts constitute a cogent argument against the uncritical application of this method of treatment. However, the fact that several investigators advise limited periods of anticoagulant therapy in various nonhemorrhagic cerebrovascular disorders indicates that there is something to be said for this form of treatment. There is a need for a controlled trial of long-term anticoagulant therapy in carefully selected cases of intermittent insufficiency in the carotico-vertebral systems, in vertebro-basilar thrombosis and in advancing carotid occlusion, for it is these patients who may be most benefited with the least risk.

TREATMENT OF A CASE OF HEMOPHILIA A WITH PORCINE ANTIHEMOPHILIC GLOBULIN

A 49-year-old patient with a history of previous severe hemorrhages developed a hematoma at the base of his tongue after a coughing spell. Fischer, Cancura and Deutsch (*Wien. klin. Wchnschr.*, 73, 312, 1961) report that its size increased rapidly, and on admission to hospital the patient was in severe respiratory distress owing to obstruction of mouth and pharynx by the huge hematoma. Inspection of the larynx and intubation were not possible, and ordinarily a tracheotomy would have been done at once. In hemophiliacs, however, this procedure has a mortality rate of 50%, and it was decided to avoid it if at all possible.

Laboratory tests revealed absence of factor VIII, and the diagnosis of hemophilia A was made.

Oxygen was administered through a nasal catheter which was advanced as far toward the larynx as possible, and 320 c.c. of fresh blood and 2 units of antihemophilic plasma were given. In spite of this the hematoma continued to increase in size, and severe choking spells developed. Several quarts of antihemophilic plasma would have been required to stop this bleeding, more than could have been given safely over a short period of time without overloading the circulation.

In this critical situation it was decided to use porcine antihemophilic globulin (PAG), and 200 Oxford units was administered together with 25 mg. of a cortisone preparation to avoid an anaphylactic reaction. The respiratory distress did not increase further, and within the next six hours three additional doses of PAG were given. At the end of that time the thromboplastin regeneration test had become normal, and the bleeding had apparently stopped. From then on PAG was given every eight hours, while steady improvement continued. On the eighth day it was replaced by human antihemophilic plasma to avoid an allergic reaction. The further progress was uneventful. Human antihemophilic globulin is not stable, and its concentration in the plasma is low. In spite of these difficulties Swedish scientists have succeeded in producing a therapeutic preparation which, however, is not yet available on the market. In desperate situations it may therefore be necessary to resort to PAG.

ARE GALLSTONES AND GALLBLADDER CARCINOMA RELATED?

To test the concept which has often been reported in the literature that gallstones are related to gallbladder carcinoma, Derman *et al.* (*J. A. M. A.*, 176: 450, 1961) reviewed 1396 consecutive cholecystectomies between January 1948 and June 30, 1960.

It was found that: (1) the incidence of primary carcinoma of the gallbladder was 1.4% (19 of 1396 cholecystectomy specimens); (2) only three true adenomatous polypi were present in the series; (3) there were no carcinomas of the gallbladder in patients under 50 years of age, but over age 50 the incidence of carcinoma was 2.4%; (4) in the entire series the incidence of cholelithiasis was 86.9%; (5) the incidence of carcinoma in the presence of gallstones was 1.2% of the total series, and 2.2% of the series over 50 years of age; (6) the incidence of carcinoma in the absence of gallstones was 2.2% of the total series, and 4.3% of the series over age 50. The difference between the incidence of carcinoma with and without stones was not significant.

In summary, the authors conclude that gallbladder carcinoma is not related to the presence of gallstones, and the fact that there were fewer polypi than carcinomas offers no support for the concept that gallbladder polypi are premalignant lesions. There would therefore be no justification for the prophylactic removal of a gallbladder containing stones or polypi for the purpose of preventing malignancy.

(Continued on advertising page 35)

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MEDICAL SOCIETIES

NEW SECTION OF CANADIAN ASSOCIATION OF PATHOLOGISTS

Diagnosis of malignant disease and of some endocrine disorders by the study of exfoliated cells has been a most important advance in laboratory techniques of this generation. Because of its particular application to the cancer of the female genital tract, cytodiagnosis has found exponents amongst gynecologists and allied workers as well as amongst pathologists. The new specialty has now developed to a point where a scientific society is urgently needed.

Recently, a group of medical cytologists approached the Canadian Association of Pathologists with the suggestion that they should associate themselves with the Canadian Association of Pathologists. The constitution of the Canadian Association of Pathologists has accordingly been amended to allow the setting up of sections devoted to cytology and other allied disciplines.

On July 12, 1961, a meeting between representatives of the Canadian Association of Pathologists and of the cytologists was held in Ottawa in order to establish the Section of Cytology. This organizing Committee has suggested that the section be known as, "The Canadian Cytology Council: A Section of The Canadian Association of Pathologists". The first meeting of the Council will be held on October 21 at Prudhommes' Garden Centre, St. Catharines, Ontario, in conjunction with the annual meeting of the Ontario Association of Pathologists.

Membership of the Council will be open to all members of the Canadian Association of Pathologists, to medical cytologists and to clinicians actively interested in cytology. All qualified medical scientists are eligible for full membership in the section of cytology, and non-pathologists are eligible for associate membership in the Canadian Association of Pathologists.

It is hoped that all medical workers in this field, including physicians and surgeons whose specialty utilizes cytodiagnosis, will take an active part in the formation and development of the Council.

Those who are not already Members or Associate Members of the Canadian Association of Pathologists and who wish to join the new organization should forward their applications immediately to the Secretary, Dr. D. W. Penner, Winnipeg General Hospital, Winnipeg 3, Manitoba.

PUBLIC HEALTH

SURVEILLANCE REPORT OF EPIDEMIC OR UNUSUAL COMMUNICABLE DISEASES

Poliomyelitis Trends, 1960

Paralytic poliomyelitis (080.0, 080.1) is a virus disease that gains in strength with the advance of the summer season, attacking in its course people of all ages but particularly those under 40 and more particularly those under 20 years of age. This was the experience of the decade from 1951 to 1960. In other respects the disease has been variable, some years reaching an epidemic level for the country as a whole, some years falling far short, with the rate of incidence of the new cases in one province often greatly different from that in another.

The course of the disease in 1960 illustrates these points: there were more cases in the ninth 4-week period (the first 4-week period in 1960 ended on January 30) than in any other period of the year; the highest attack rate appeared in the age group four years and under; the overall rate of 5.1 cases per 100,000 was less than half the rate of the previous year, yet in four provinces the 1960 rate was higher than that for 1959. (Age is not reported for all provinces.)

The seasonal incidence of new cases in 1960 reached its highest levels in the eighth, ninth and tenth 4-week periods. Seven times altogether in the past 10 years these have been the three periods in which the most cases occurred. While the last 24 weeks have always accounted for the majority of cases, the first 28 weeks have on occasion contributed substantially to the year's total; 1960 was an example of this, with 28% of the cases coming in the first 28 weeks of the year. In contrast, in 1959 there were 7% of cases, only, in this period.

The effect of paralytic poliomyelitis for a number of years on people of different ages is shown in some detail in the accompanying table—for six provinces for which this information was continuously available.

The truth of the statement that the disease attacks most strongly the younger age groups is evident. It is also evident that the effect on one age-group relative to any other varies both from year to year and from province to province. For the six provinces considered as a group the total rate for those four years and under was, in round terms, six times the rate of those 20 and over in 1951, nine times in 1959 and six times in 1960. In the same round terms the total rate for those in the 5-14 age group was seven, three and four times the 20 plus rate in 1951, 1959 and 1960, respectively. In Newfoundland the four years and under rate in 1960 was more than 50 times as great as the 20 plus rate; in British Columbia it was between three and four times the rate of the older age group.

The average yearly rate per 100,000 persons for poliomyelitis for all Canada for the 10 years 1951-60 was eight cases. (In 1952 and 1953, Alberta did not report paralytic poliomyelitis separately.) The Canada rate in those 10 years reached a maximum of 28.3 in 1953 and a minimum of 1.1 in 1957. The highest provincial rate recorded in the decade was that of 182.9 for Manitoba in 1953. In that year the New Brunswick rate was only 2.4 per 100,000. In 1960 the Manitoba rate was 1.4, the New Brunswick rate 15.3.

Differences in rate of seasonal advance, fluctuations in intensity in time and in place, these are the highly variable features of paralytic poliomyelitis; concentration in the summer reaching a peak in the ninth 4-week period of the year, highest incidence among the younger age groups, these are the constant features of the disease in the last 10 years.

Prepared in the Health and Welfare Division, Public Health Section, Dominion Bureau of Statistics.

PARALYTIC POLIOMYELITIS: AGE-SPECIFIC CASE RATES PER 100,000 POPULATION

	All ages			Age group: 4 years and under			5 - 14			15 - 19			20 years and over		
Province	1951	1959	1960	1951	1959	1960	1951	1959	1960	1951	1959	1960	1951	1959	1960
Total	2.9	8.4	9.9	5.8	29.6	26.8	6.8	11.1	15.7	4.1	5.2	9.7	1.0	3.3	4.2
Newfoundland	1.1	31.0	10.7	—	125.0	47.4	3.6	31.4	7.6	—	19.7	9.3	0.5	2.7	0.9
New Brunswick	2.9	9.5	15.2	5.3	21.5	24.1	8.3	13.5	34.8	2.3	5.7	18.1	0.3	5.4	3.7
Manitoba	4.2	2.9	1.4	12.2	15.3	5.7	10.5	1.1	2.7	5.3	—	1.5	1.0	1.5	0.2
Saskatchewan	6.9	5.0	6.2	12.0	17.7	16.7	14.8	4.7	10.8	7.3	4.2	9.5	3.3	2.5	1.7
Alberta	2.3	6.7	15.7	4.3	18.8	42.6	4.1	10.4	23.7	6.8	2.2	12.6	0.9	3.0	6.6
British Columbia	0.1	8.0	10.1	0.8	21.6	23.1	—	12.9	13.7	—	5.8	8.3	—	4.2	6.8

—No cases reported.

PARALYTIC POLIOMYELITIS: CASES AND RATES PER 100,000 POPULATION, BY PROVINCES, 1951 - 60

Year	Canada	Nfld.	P.E.I.	N.S.	N.B.	Que.	Ont.	Man.	Sask.	Alta.	B.C.	Yukon	N.W.T.
	Cases												
1951	1220	4	13	205	15	247	619	37	57	22	1		
1952	1595	2	56	41	67	123	269	410	447	[1]	180		
1953	3912	162	6	25	13	477	985	1480	357	[1]	407		
1954	1456	14	49	63	7	791	94	66	41	221	110		
1955	584	12	11	55	6	119	75	15	20	125	146	—	
1956	400	3	3	9	7	156	127	15	7	35	37	1	
1957	182	1	—	—	5	37	54	8	20	31	26	—	
1958	249	4	—	—	4	79	20	107	1	22	12	—	
1959	1886	139	7	9	62	1171	200	26	46	83	132	1	10
1960	909	49	1	9	92	284	39	13	56	201	165	—	..
	Rates[2]												
1951	8.7	1.1	13.2	31.9	2.9	6.1	13.5	4.8	6.9	2.3	0.1		
1952	11.8	0.5	56.0	6.3	12.7	2.9	5.6	51.4	53.0	[1]	14.9		
1953	28.3	42.3	5.9	3.8	2.4	11.2	19.9	182.9	41.5	[1]	32.6		
1954	9.5	3.5	48.5	9.4	1.3	18.0	1.8	8.0	4.7	20.9	8.5		
1955	3.7	3.0	11.0	8.1	1.1	2.6	1.4	1.8	2.3	11.5	10.9	—	
1956	2.5	0.7	3.0	1.3	1.3	3.4	2.3	1.8	0.8	3.1	2.6	8.2	
1957	1.1	0.2	—	—	0.9	0.8	1.0	0.9	2.3	2.7	1.7	—	
1958	1.5	0.9	—	—	0.7	1.6	0.3	12.3	0.1	1.8	0.8	—	
1959	10.8	31.0	6.9	1.3	10.5	23.4	3.4	2.9	5.1	6.7	8.4	7.7	47.6
1960	5.1	10.7	1.0	1.2	15.3	5.6	0.6	1.4	6.2	15.7	10.3	—	..

[1]Cases in Alberta not reportable by type.
[2]Excluding provinces which did not report.
—No cases reported.
..Figures not available.

PARALYTIC POLIOMYELITIS IN CANADA*
32ND WEEK—ENDING AUGUST 12, 1961

	Reported cases: This week			Reported cases: Last week			Reported cases: To this date			Deaths: To this date		
	1961	1960	1959	1961	1960	1959	1961	1960	1959	1961	1960	1959
Canada	8	61	132	4	42	128	60	451	535	2	31	45
Newfoundland	—	3	7	—	1	6	—	33	50	—	2	4
Prince Edward Island	—	—	—	—	—	—	—	1	—	—	—	—
Nova Scotia	—	—	—	—	1	—	—	7	1	—	1	—
New Brunswick	—	5	1	—	4	2	1	55	8	—	—	1
Quebec	2	19	110	4	9	105	23	109	393	—	12	30
Ontario	4	3	6	—	4	9	10	11	36	—	—	4
Manitoba	—	1	1	—	1	1	—	8	8	—	—	—
Saskatchewan	—	4	1	—	8	2	2	34	11	—	3	1
Alberta	2	11	4	—	7	3	21	73	12	2	4	1
British Columbia	—	15	2	—	7	—	3	120	5	—	9	—
Yukon	—	—	—	—	—	—	—	—	—	—	—	—
Northwest Territories	—	—	—	—	—	—	—	—	11	—	—	4

*Weekly returns based on telegraphic reports by provinces.

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BOOK REVIEWS

MODERN TRENDS IN CARDIOLOGY. Edited by A. Morgan Jones. 264 pp. Illust. Butterworth & Co. (Publishers) Ltd., London; Butterworth & Co. (Canada) Ltd., Toronto, 1961. $14.50.

It is all too seldom that a reviewer finds himself in the happy position of being able to give almost unqualified approval to a book; but as this reviewer progressed with increasing satisfaction from chapter to chapter of this symposium he began to feel the cautious stirrings of a hope that he might end up in just such a position, and at the conclusion of the 16th and final chapter he had to concede that this hope was amply fulfilled.

Most of the 19 contributors are leading British cardiologists, but there are in addition five prominent Americans and a Swede. It is a tribute to the firm direction of the editor that most of the 16 chapters, although written by different individuals, display similar authority, clarity and conciseness. The range of subject matter extends through metabolism of heart muscle, cardio-respiratory function tests, renal changes in heart disease, theories of clotting, to the clinical and laboratory diagnosis and the management and prognosis of the various categories of heart disease. In each case the argument proceeds logically and directly from physiological considerations to clinical application.

The scope and intent of the book may be suggested by a short quotation from the Editor, Prof. A. Morgan Jones of Manchester:

"To define trends of thought in a subject is not synonymous with free speculation upon the nature of future developments; but it does imply a careful consideration of the direction in which ideas have changed in the last decade, an evaluation of current unsolved problems, and some discussion of the methods available to solve them."

Actually the book does more than this, offering in addition a comprehensive survey of present-day concepts in almost every phase of heart disease.

SOME ASPECTS OF OBLITERATIVE VASCULAR DISEASE OF THE LOWER LIMB. J. A. Gillespie and D. M. Douglas. E. & S. Livingstone Ltd., London; The Macmillan Company of Canada Limited, Toronto, 1961. $5.00.

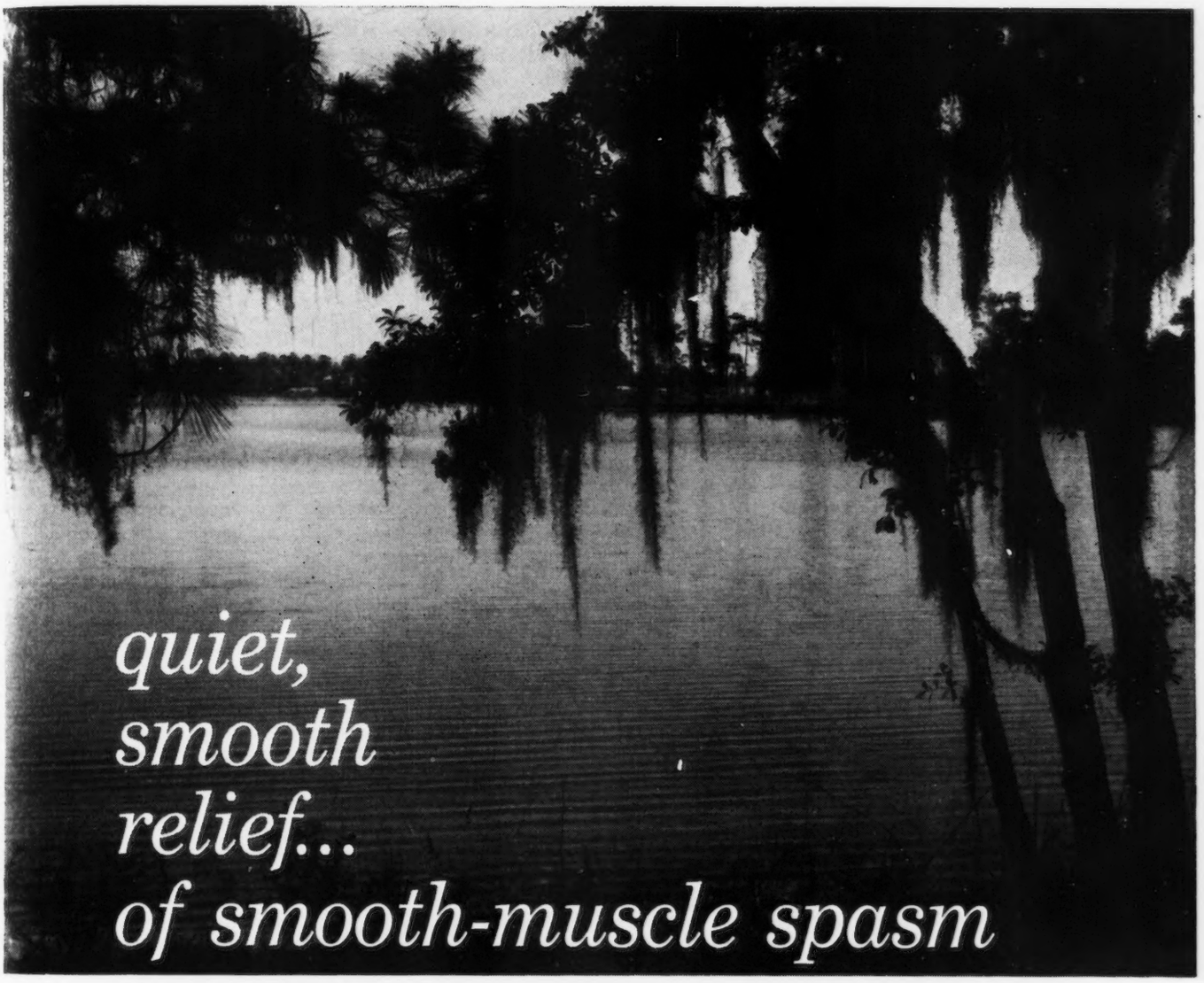
This interesting monograph contains useful information on the effects of treatment on patients with obliterative vascular disease. The chapters on the use of vasodilators and lumbar sympathectomy are especially good. Unfortunately, the authors state that this book is primarily for those not familiar with the field of peripheral vascular disease, and some of their statements are rather dogmatic for the more inexperienced. For instance, the authors recommend that arteriography be carried out in every patient being investigated for peripheral vascular disease but give little guide as to when such patients should be investigated. Many patients with mild claudication do not require arteriography when first seen by their doctor. Also, 20 pages on the physiological effects of lumbar sympathectomy on sudomotor activity is strong diet for those not specializing in peripheral vascular disorders. The position of the patient for lumbar symphathectomy as depicted in one of the illustrations of operative technique (Fig. 6, 4) can be avoided by use of a simple supine position with small sandbags under the chest and buttock of the side being operated upon. Such a position gives good exposure and is certainly much more comfortable and probably considerably less dangerous for the elderly patient than the one depicted.

The reviewer gets the impression that this monograph will be read and enjoyed much more by the physician or surgeon who specializes in peripheral vascular disorders than those who do not. Illustrations and diagrams are numerous and well chosen, and the publishers have maintained the high quality of reproduction that one has come to associate with their name.

IONIZING RADIATION AND HEALTH. World Health Organization Public Health Papers No. 6. Bo Lindell and R. Lowry Dobson. 81 pp. World Health Organization. Geneva; Columbia University Press, New York, 1961. $1.00. Also published in French.

The subject of ionizing radiation and its effects on health is of tremendous interest and importance to both the medical profession and non-medical people. This book, a condensation of recent work and ideas on this subject, begins with a short chapter on the biological effects of ionizing radiation. The significance of dose rate is discussed. This has a tremendous bearing on the effect of radiation. The authors refer to the intense medical research program that is being carried out to attempt to provide human data on the possible effects of small doses of radiation and a chronic low level of radiation. They discuss natural sources of radiation. The radiation from medical exposures of x-ray diagnostic examinations and x-ray therapy, including the use of radioactive isotopes, is very well covered. A number of tables provide the details of gonadal exposures from various types of diagnostic examinations. Attempts should be made to reduce exposure from medical radiography only after clearly and carefully studying the effect on the particular ex-

(Continued on page 718)



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Research in the Service of Medicine

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amination being considered. The potential beneficial effect must be carefully weighed against any possible deleterious effect.

Radioactive fallout is discussed briefly.

Excerpts from reports of the International Commission on Radiological Protection and the International Commission on Radiological Units and Measurements are included in Annex 1. An excellent glossary of technical terms is provided in Annex 2.

This short book is an excellent summary of what is currently known about ionizing radiation. It should be read by everyone in the medical profession and all others who are particularly interested in radiation and its effects.

CHEMISTRY OF DRUG METABOLISM. A Monograph in The Bannerstone Division of American Lectures in Living Chemistry. William H. Fishman. 235 pp. Illust. Charles C Thomas, Springfield, Ill., 1961. $10.50.

This book presents a scholarly review of present knowledge concerning the fate of foreign organic compounds in the animal organism, and for this reason will be of value to the biochemist and pharmacologist and to the clinician whose interests lie close to these fields. The book is primarily concerned with the metabolic pathways of drugs and organic chemicals with particular emphasis on metabolic conjugations, especially on the glucuronic acid conjugation and glucuronic acid biochemistry.

A review of the metabolic transformations of foreign organic compounds such as benzene, polycyclic hydrocarbons, alkylbenzenes and others, and drugs such as salicylates, barbiturates, morphine, sulfonamides and so on, is presented in a clear, concise and well-documented manner and provides the facts necessary for a discussion of the biochemical mechanisms by which the metabolic transformations are accomplished. This section is followed by one on the subject of metabolic conjugations.

As an outcome of this survey, the author suggests certain correlations between the metabolism of ascorbic acid, the hydroxylation of drugs, the action of certain hormones, alterations in beta-glucuronidase activity and connective tissue. This provocative synthesis of previously isolated facts serves to round out the book and offer opportunities for further research work.

ABDOMINAL OPERATIONS. With Special Articles by 36 British and American Contributors. 4th ed. Rodney Maingot. 1402 pp. Illust. Appleton-Century-Crofts, Inc., New York, 1961. $29.50.

In the 4th edition of his book on abdominal operations, Mr. Maingot has drawn upon the experience of several authorities from both the United Kingdom and the United States.

This book contains a most exhaustive description of almost every condition in the abdomen that one can envisage. There is an excellent general description of all of these different diseases and conditions from the point of view of their etiology, diagnosis, and other features of interest, and this is followed by a detailed description of the management of such cases, particularly their operative management. The author borrows from his own vast experience and supplements this with views expressed by other authorities, some of which may be divergent to his own.

The bibliography is very extensive, and references to articles in the literature are freely quoted. The annotation of historical facts associated with certain procedures provides added interest.

This is a valuable book not only for the resident in training who is interested in abdominal surgery, but also for the clinical surgeon, as a reference book. The undergraduate in medicine, too, will find this book useful as a reference text.

This volume should be on the bookshelf of every surgeon who is interested in abdominal surgery, and also in reference libraries for the use of residents training in surgery.

DERMATOLOGIE UND VENEROLOGIE. Einschliesslich Berufskrankheiten Dermatologishcher Kosmetik und Andrologie. In funf Bänden. Band I, Teil 1. H. A. Gottron and W. Schönfeld. 743 pp. Illust. Georg Thieme, Stuttgart, W. Germany; Intercontinental Medical Book Corporation, New York, 1961. $46.75.

The first part of volume I was published after volumes II and III had appeared and combines the excellent features of the previous volumes but shows hardly any of their shortcomings. The major chapters, "Anatomy of the Skin" (E. Horstman), "Physiology" (H. Göpfert) and "General Pathology" (G. K. Steigleder), are very well organized, comprehensive treatises. Even more impressive are some of the chapters dealing with special matters. Dr. Schulze writes on percutaneous absorption, Dr. Kleine-Natrop on skin temperature and its measurement and on physical testing methods; these are most thorough monographs, of great value to the student as well as to any research worker in these fields. Braun-Falco provides a comprehensive survey on histochemical methods and findings in skin diseases; Leinbröck deals competently with electrophoresis in dermatology; W. H. Spier discusses allergy of the skin; and Burckhardt describes test methods of value in dermatology. All chapters are particularly well organized, are well illustrated and have a comprehensive index and an up-to-date listing of literature references which include, in contrast to some of the previously published volumes, an adequate selection of the North American literature.

This volume would be a useful addition to any large medical library.

MEDICAL NEWS *in Brief*

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CONSERVATIVE MANAGEMENT OF BARBITURATE INTOXICATION

During the five-year period 1953 to 1958, 140 patients were admitted to a large metropolitan general hospital with a diagnosis of barbiturate intoxication. A communication by Ferguson and Grace (*Ann. Int. Med.*, 54: 726, 1961) concerns the 95 patients who were unconscious as a result of barbiturate intoxication and who represented a therapeutic problem. The series included one death.

Analysis of the data indicates that the most important aspects of the treatment are (1) the maintenance of a patent airway, (2) the maintenance of the blood pressure at a satisfactory level by the use of vasopressor agents, and (3) the most meticulous nursing care, with special attention being paid to the vital signs, to the patient's posture, and to the eyes, skin and tongue.

Only one of the patients in this group received a therapeutic dose of a stimulating drug. The other 94 received no such treatment. Gastric lavage was carried out in many. There was nothing to suggest that this measure was beneficial. On the other hand, five of the patients subjected to gastric lavage aspirated gastric content. In two of these, the result of obstruction of the airway was sufficiently severe to justify tracheotomy. In two others, vasomotor collapse followed gastric intubation.

Despite the fact that there were numerous instances of prolonged coma, elective tracheotomy was considered to be necessary on one occasion only. Penicillin and other antibiotics were administered "prophylactically" to 61 patients. Pneumonia developed in two of these patients and fever in 12 others. The group included one case of pneumonia in which no antibiotic was used.

The mortality figures in this series of patients are much more favourable than the figures reported by other authors for series of patients subjected to vigorous analeptic therapy.

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MEDICAL NEWS *in brief*

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ORAL POLIO VACCINE CLEARED BY U.S.

The U.S. Government has announced clearance of oral poliomyelitis vaccine for protection against Type I poliomyelitis. Announcing the granting of a licence to manufacture the live vaccine (Type I), Surgeon-General Luther L. Terry of the Public Health Service emphasized that it was of the highest importance that vaccinations continue with the Salk vaccine which is the only weapon available to provide protection against all three types of poliomyelitis.

Type I poliomyelitis virus has been responsible in recent years for between 60 and 70% of all paralytic poliomyelitis in the United States. It is expected that Type II oral vaccine will be licensed in the near future, but that it will be several months at least before Type III is cleared. The Type I licence was issued to Pfizer Ltd., Sandwich, England.

To date this year in the United States less than 300 paralytic cases have been reported. This compares with 13,860 for the poliomyelitis season of 1955, the first year in which the Salk vaccine became available in limited quantities.

AMERICAN COLLEGE OF PHYSICIANS: POSTGRADUATE COURSES, AUTUMN-WINTER, 1961-62

The American College of Physicians has scheduled the following postgraduate courses for the autumn-winter session, 1961-62:

Course No. 1, *Changing Concepts of Cardiopulmonary Disease*, Ohio State University Health Center, Columbus, Ohio, September 18-23, 1961.

Course No. 2, *The Physiologic Basis of Internal Medicine*, Duke University Medical Center, Durham, N.C., October 9-13, 1961.

Course No. 3, *The Internist's Role in the Preoperative and Postoperative Care of the Surgical Patient*, Mayo Clinic, Rochester, Minn., November 6-10, 1961.

Course No. 4, *Advances in Electrocardiography* , New York University Medical Center, New York, N.Y., December 4-8, 1961.

Course No. 5, *Internal Medicine —Today's Problems in Diagnosis and Management, and Tomorrow's Projections*, Ochsner Foundation Hospital, New Orleans, La., January 15-18, 1962.

Course No. 6, *Medical Genetics*, The University of Michigan Medical School, Ann Arbor, Mich., January 29-February 1, 1962.

Course No. 7, *Pathologic Physiology of the Blood Dyscrasias*, Washington University School of Medicine, St. Louis, Mo., February 12-16, 1962.

Course No. 8, *Symposia on Challenging Medical Problems*, Baylor University College of Medicine, Houston, Texas, February 19-23, 1962.

All courses have been arranged through the co-operation of the institutions at which the courses will be given. Tuition fees: Members, $60.00; non-members, $80.00. Registration forms and requests for information should be addressed

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MEDICAL NEWS *in brief*
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to: Edward C. Rosenow, Jr., M.D., Executive Director, American College of Physicians, 4200 Pine Street, Philadelphia 4, Pa.

ANNOUNCEMENT OF SUPPORT FOR CAREER INVESTIGATORS IN LEUKEMIA RESEARCH

A program of five-year support for career investigators in leukemia research has been announced by The Leukemia Society of New York. The amount of $10,000 to $15,000 will be awarded per annum for five years, renewable to ten years, to qualified investigators in basic science of clinical departments of medical schools, universities and research institutes.

The Leukemia Society Scholar whose research is broadly related to the problem of leukemia is expected to serve as a regular member of the faculty or staff of his institution.

Nominations for 1962 should be submitted no later than November 1, 1961, to The Leukemia Society, Inc., 405 Lexington Avenue, New York 17, N.Y., U.S.A.

NOTICE OF NATIONAL CANCER INSTITUTE OF CANADA RESEARCH GRANTS

The National Cancer Institute of Canada offers financial support for new as well as established worthy research projects which may be related to a furthering of general knowledge concerning cancer. Such grants are made to individuals with research experience for the purchase and maintenance of animals and equipment, for expendable supplies and for the payment of technical and research assistants.

Limited expenses incurred by travelling for scientific purposes are considered separately, and requests for such should be submitted to the Executive Director. In general, such travelling grants will be made for the purpose of presenting a paper at a scientific meeting or of learning a new technique in cancer research.

Research grants commence on April 1 and terminate on March 31. Application forms may be obtained from the Institute and six copies should be submitted by December 15. They should always be completed in a detailed manner so that the referees may make a comprehensive appraisal of the project or its progress and the intended use of the research grant.

Address all communications to: Executive Director, National Cancer Institute of Canada, 790 Bay Street, Toronto 2, Ontario.

1961 WALTER W. WRIGHT LECTURE: UNIVERSITY OF TORONTO

The Walter W. Wright Lectureship, under the joint sponsorship of the Department of Ophthalmology and the Faculty of Medicine, University of Toronto, will be given by Dr. Michael J. Hogan at the Toronto General Hospital on November 17, at 4:00 p.m. The title of Dr. Hogan's address will be "Present Knowledge of the Etiology of Iritis". Previous to the lecture the Alumni of the Department of Ophthalmology of the University of Toronto will hold their annual clinical meeting. In the evening there will be a banquet and dance at the Royal York Hotel.

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Books Received

Books are acknowledged as received, but in some cases reviews will also be made in later issues.

Psychosomatic Aspects of Paediatrics. Study Group of the Society for Psychosomatic Research held at the Royal College of Physicians, May 1959. Edited by Ronald MacKeith and Joseph Sandler. 155 pp. Pergamon Press Ltd., Oxford; Pergamon Press, Inc., New York, 1961. 50s. net.

Calderwood's Orthopedic Nursing. 5th ed. Carroll B. Larson and Marjorie Gould. 547 pp. Illust. The C. V. Mosby Co., St. Louis, Mo., 1961. $6.50.

Applied Dental Anatomy. Nicholas J. Brescia. 212 pp. Illust. The C. V. Mosby Co., St. Louis, Mo., 1961. $7.50.

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ANNOUNCEMENT OF CONFERENCE ON OBESITY

An exploration into the serious problem of obesity among teenagers will be the subject of a symposium sponsored by the American Medical Association's Council on Foods and Nutrition.

The one-day conference will be held at Stanford University, Stanford, Calif., U.S.A., on Saturday, October 21. Co-sponsors include the Department of Pediatrics of the Stanford School of Medicine, California State Department of Health, California Medical Association, and Santa Clara and San Mateo County Medical Societies.

The conference moderator will be Dr. Norman Kretchmer, Stanford University School of Medicine. The dean of the School of Medicine at Stanford, Dr. Robert H. Alway, will deliver opening remarks.

The morning session will deal with fat metabolism and various aspects of weight control. Psychological aspects of overeating and obesity, evaluation of caloric needs, and a panel discussion of the obese adolescent, will conclude the program.

Participants include Drs. Harold Harper, University of California School of Medicine, San Francisco; William Parson, University of Virginia School of Medicine, Charlottesville; Edmund Volkart, Stanford University; Hilde Bruch, Columbia University College of Physicians and Surgeons, New York; Dr. Josef Brozek, Lehigh University, Bethlehem, Pa.

In addition to Drs. Bruch and Volkart, panel participants are Drs. Harry Jennison, Stanford University School of Medicine; Leslie Corsa, Jr., California State Department of Public Health, Berkeley; Luigi Luzzatti, Stanford University School of Medicine.

Advance registration may be made with the Council on Foods and Nutrition, American Medical Association, 535 North Dearborn, Chicago 10, Illinois, U.S.A.

POSTGRADUATE COURSE ON EMERGENCIES IN GENERAL PRACTICE

A postgraduate course on emergencies, sponsored by the Medical Alumni Association of the University of Toronto, will be given at Sunnybrook Hospital, Toronto, on October 11, 12 and 13, 1961. No advance registration is required. Credits will be given members of the College of General Practice (Medicine) of Canada on an hour-for-hour basis of actual lecture time.

REFRESHER COURSE IN MALIGNANT DISEASE, BRITISH COLUMBIA CANCER INSTITUTE

A Refresher Course in Malignant Disease, sponsored by the British Columbia Cancer Institute, will be held in Vancouver from October 10 to 13, 1961. The guest speakers will be Sir Stanford Cade and Sir Peter Dixon, of London, England, and Dr. Arthur T. Hertig of Boston, Mass.

Applications should be addressed to Dr. A. M. Evans, Director, British Columbia Cancer Institute, 2656 Heather Street, Vancouver 9, B.C. There is no fee.

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REPRODUCTION OF CHEST RADIOGRAPHS PROVIDES NEW APPROACH TO CONTROL OF DUST DISEASES

Fully satisfactory copies of radiographs of the chest have been produced for the first time on a large scale and will be given worldwide distribution by the International Labour Office.

The problem of reproducing, with great fidelity, sets of standard radiographs came to the fore with the establishment, in 1958, of a new international classification for the radiological appearances of pneumoconiosis.

The need for an international classification providing a uniform basis of comparison has long been felt. Four meetings of experts on pneumoconiosis have been convened by the ILO to grapple with this problem. The first was held at Johannesburg, South Africa, in 1930; the second, at Geneva in 1938; the third, at Sydney, Australia, in 1950, and the fourth, at Geneva in 1958.

The 1958 meeting was attended by 12 experts from 10 countries. These experts succeeded in establishing a single international classification for the radiological appearances of all the pneumoconioses caused by mineral dusts. Pneumoconioses of vegetable origin, radiologically very different, had to be excluded.

The object of the classification is to codify the radiological appearances of the pneumoconioses in a simple, easily reproduced way and thus to facilitate the statistical and epidemiological investigations undertaken as part of the search for effective measures to control the disease on an international basis.

The classification is not intended to define pathological entities or to measure individual working capacity; nor was it intended to be a method of assessment for compensation.

The experts agreed in 1958 that their verbal descriptions were not enough. Standard films illustrating the various radiographic appearances defined in the classification were recognized as necessary.

It was decided at the meeting that the job of selecting master copies for the definitive set of standard radiographs should be given to a small group of experts

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working in close collaboration with the ILO. The group consisted of Dr. A. I. G. McLaughlin, Deputy Director, Department for Research in Industrial Medicine, British Medical Research Council, London Hospital; Dr. V. Van Mechelen, Medical Director, Institut d'hygiène des mines, Hasselt, Belgium, and Prof. A. L. Cochrane of the Pneumoconiosis Research Unit of the British Medical Research Council. W. G. Clarke, expert radiographer of the Pneumoconiosis Research Unit of the British Medical Research Council, assisted the working group on the technical side. The reproductions themselves were made by Gevaert Photo-Production of Antwerp, Belgium.

The thorniest technical problem involved was that of reproducing radiographs without any increase in contrast and consequent loss of detail. Techniques developed during World War II for the reproduction of aerial photographs helped provide the answer. The use of an electronic scanner combined with the careful control of development times and a good deal of trial and error produced in the end a series of copies described by the experts as the best of their kind anywhere in the world. They have been pronounced superior to many original radiographs.

Sets of 14 standard productions are now being sent by ILO to interested parties throughout the world. A description of classification in English and French is enclosed with each set. Since slight variations still sometimes occur, no reproduction is certified for dispatch until it has been carefully checked for fidelity with the original. The present operation is the first involving an international distribution of reproductions of radiographs.

Sets of standard films may be ordered from the Canada Branch Office of the International Labour Office, 202 Queen Street, Ottawa 4, at a cost of $25.00 each.

WHIPPLE'S INTESTINAL LIPODYSTROPHY

In 1907, Whipple described a disease in a 36-year-old male, characterized by steatorrhea, debility, loss of weight, anemia, polyarthritis and cough. Since that time, 69 cases of the same entity have been reported with pathologic proof. The disease is frequently considered in the differential diagnosis of syndromes of intestinal malabsorption.

The seventieth case of Whipple's disease has been reported by Jaffe (*Ann. Int. Med.*, 54: 776, 1961). It is of unusual interest because recurrent fever and polyarthritis were the only clinical features over a period of 13 years. The diagnosis was established by laparotomy performed because of the development of a palpable abdominal mass. At operation, the small intestine was thickened and rubbery in consistency. The mesentery was, in great part, replaced by indurated fatty tissue and enlarged mesenteric nodes filled with fat. The histologic examination revealed characteristic macrophages (foam cells), which stained positively with periodic-acid-Schiff (PAS) stain. This indicates the presence of glycoprotein in the macrophages and represents histologic corroboration of the diagnosis. Intestinal malab-

sorption, though not clinically manifested in this patient, was demonstrated by studies with I^{131}-labelled triolein. The patient received adrenal steroid therapy in the hope that the morbid process could be arrested. In fact, the treatment brought about a subsidence of fever, and the joint pain disappeared completely.

The pathogenesis of Whipple's disease is not known, but probably the clinical characteristics are a result of the formation of abnormal glycoprotein. This material can produce malabsorption by mechanical blockage of the lacteals. The systemic symptoms of fever, arthritis, and polyserositis probably represent a hypersensitivity to this abnormal protein.

NEW OFFICIALS IN CANADIAN SOCIETY OF LABORATORY TECHNOLOGISTS

Miss Ileen Kemp, Executive Secretary of the Canadian Society of Laboratory Technologists for many years, retired from office at the end of August. She was replaced by Mr. Byron F. Wood. Mr. Wood has been with the Society as Registrar for over a year. In that period, through his work with the Certification Board, he has greatly furthered the development of the Society's new certification program. In the post of Secretary, he will be able to make additional use of the experience he has gained in the standards area and in business.

The post of Registrar is being filled by Mr. A. R. Shearer. Mr. Shearer brings a wide knowledge of laboratory services in Canada from over 25 years of experience. He also brings a wealth of experience in administration and in the aims and ideals of the Society to which he has been a major contributor for many years.

Miss Kemp will remain in the office until the end of December in order to assist the new officials.

MARKLE SCHOLAR GRANTS TO CONTINUE

The John and Mary R. Markle Foundation will continue for the fifteenth year its program of five-year grants for Scholars in Medical Science. Accredited medical schools have been invited to nominate candidates, one for each school, by December 1 for the twenty-five $30,000 grants that begin in 1962.

The letters of invitation from the President, John M. Russell, stress the point that the Foundation encourages the use of the grants as "free funds". They need not necessarily be allotted for salary, but may be used for any purpose within the policies of the medical school that will contribute to the growth of the Scholar as teacher and investigator.

Since 1948, when the program began, over 300 teachers and investigators in 78 medical schools have been assisted by Scholar grants, through appropriations of over $9,000,000. A booklet describing the grants is available from the Foundation, 511 Fifth Avenue, New York 17, N.Y., U.S.A.

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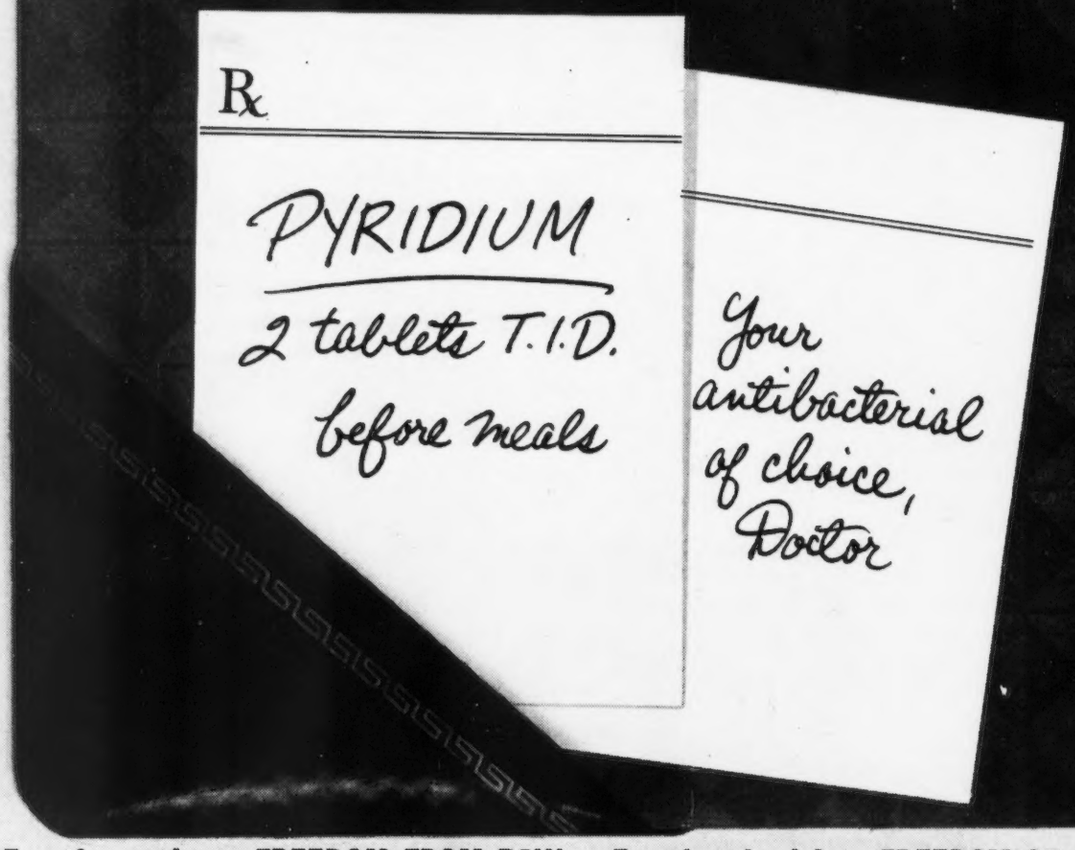

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MEDICAL NEWS *in brief*

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IODIDE "MUMPS"

In two cases of acute parotid swelling following oral ingestion of iodides reported by Carter (*New England J. Med.*, 264: 987, 1961) symptoms appeared about 12 hours after the ingestion of very small amounts of iodides, and subsided in less than 72 hours.

"Iodism" is not rare as a complication of the use of iodide salts and compounds in medical therapy and diagnostic procedures, and some type of iodism will occur in most patients if a sufficiently large dose of iodides is received. The cases presented are unusual because of the symptoms and rapid onset after small doses of the drug. A review of the literature appears to indicate that acute parotitis is a very infrequent manifestation of "iodism" or iodine idiosyncrasy, particularly so when the rapid onset after such small doses of iodides (the equivalent of 30.8 mg. and 24 mg. of iodine, respectively, in the two cases described) is considered.

Iodide "mumps", although an unusual cause of painful and acute enlargement of the salivary glands, should be considered in the differential diagnosis of acute painful parotitis. Inquiry about iodide therapy or diagnostic procedures may prevent the use of expensive or unnecessary medication, and of embarrassing and tedious investigation.

UNPREDICTABILITY OF ANTIBODY RESPONSE IN INFANTS TO SALK VACCINE

Serial determinations of antibody titres against the three types of poliovirus were performed before, during and after the course of inoculation in 45 normal, full-term infants with Salk vaccine in order to obtain more information about the response of infants to antigenic stimulation with poliomyelitis vaccine and the influence of passively transferred antibodies.

Salk poliomyelitis vaccine was given according to two regimens. The infants in Group A received their first injection at age 10 weeks (median), the second at 14 weeks, the third at 40 weeks, and the fourth at 60 weeks. The infants in Group B received their first injection at 6 weeks (median), the second at 10 weeks, the third at 14 weeks, and the fourth at 40 weeks.

Cramblett and Fomon (*J. Pediat.*, 58: 779, 1961) found that, in Group A, all of the infants had serum titres of neutralizing antibodies of 1:4 or greater one month after the fourth inoculation which was given at 57 to 64 weeks of age. In Group B, three of the 13 infants had titres of neutralizing antibodies less than 1:4 against one or more of the three types of poliovirus one month after the fourth injection which was given at 36 to 45 weeks of age.

Neutralizing antibodies at a serum dilution of 1:4 or greater are commonly considered to be evidence of immunity. It would appear that an appreciable number of infants, less than eight weeks of age at the time of their first Salk poliovirus vaccine injection, will not respond satisfactorily after the fourth injection. A titre of passively transferred neutralizing antibodies of 1:16 or greater at the time the first injection was given seemed to interfere with response to active immunization.
